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MCCULLAGH, E PERRY, Cleveland, Ohio	61
McKITTRICK, CARL A, Ann Arbor, Mich	553
McLAUGHLIN, EDWARD FRANCIS, Philadelphia, Pa	184
MEIROWSKY, ARNOLD, Albany, N Y	763
MILCH, HENRY, New York, N Y	282
MIRIZZI, PROF P L, Cordoba, Argentina	360
MOORE, RICHMOND L, New York, N Y	373
MOSSBERGER, JOSEPH I, CAPT, M C, Fort Bliss, Tex	933
MOYER, CARL A, Ann Arbor, Mich	553
MULLEN, THOMAS F, San Francisco, Calif	6
MUNROE, H STOKES, JR, Chailotte, N C	751
MURRAY, MARGARET R, New York, N Y	26
NELSON, O A, Seattle, Wash	159
NICHOL, WILLIAM W, MAJOR, M C, San Francisco, Calif	942
NICKEL, WILLIAM F, JR, New York, N Y	19
OPPENHEIMER, GORDON D, New York, N Y	141
PACK, G T, New York, N Y	76, 924
PARKER, EDWARD F, Charleston, S C	355
PEARSE, HERMAN E, Rochester, N Y	776
PHELPS, DORIS, Nashville, Tenn	604
PHEMISTER, DALLAS B, Chicago, Ill	610
PILCHER, LEWIS S, Newton, Mass	827
PLAUT, JULES ALAN, New Haven, Conn	43
PRITCHARD, J E, Montreal, Can	641
PULASKI, EDWIN J, New York, N Y	217
RANKIN, L M, Upper Darby, Pa	931
RAY, BRONSON S, New York, N Y	231
REED, FRANCIS A, Chicago, Ill	874

REICH, NATHANIEL E, Brooklyn, N Y	137
RHOADS, C P, New York, N Y	924
RIENHOFF, WILLIAM F, Baltimore, Md	481
RIGDON, R H, Memphis, Tenn	122, 430
RILEY, RICHARD L, New York, N Y	127
RIVER, LOUIS P, Chicago, Ill	405, 874
ROWE, M JOHN, JR, Long Beach, Calif	950
SI JOHN, FORDYCE B, New York N Y	217
SAVITSKY, NATHAN, New York, N Y	821
SCHACHNER, RUBIN J, Chicago, Ill	610
SCHRANTZ, F S, Memphis, Tenn	122
SEALY, W C, Durham, N C	851
SEWELL, ROBERT L, Rochester, N Y	155
SHACKELFORD, RICHARD T, Baltimore, Md	864
SHAPIRO, SHEPARD, New York, N Y	175
SHERMAN, IRWIN, Baltimore, Md	481
SHERWIN, BENJAMIN, New York, N Y	175
SJAARDEMA, HENDRIKUS, Los Angeles, Calif	452
SMITH, SIMMONS, Cleveland, Ohio	337
SPEED, KELLOGG, Chicago, Ill	81
STADER, OTTO, Ardmore, Pa	623
STANDARD, SAMUEL, New York, N Y	816
STARR, ARNOLD, Boston, Mass	574
STEINER, CHARLES A, Philadelphia, Pa	147
STOUT, ARTHUR P, New York, N Y	26, 801
SUTHERLAND, ROSS, Los Angeles, Calif	950
SWARTLEY, WILLIAM B, Philadelphia, Pa	184
SWEET, RICHARD H, Boston, Mass	566
TARNOWER, HERMAN, Scarsdale, N Y	700
TAYLOR, FREDERIC W, Indianapolis, Ind	426
TUI, CO, New York, N Y	412
TURELL, ROBERT, New York, N Y	637
VALK, H L, Winston-Salem, N C	860
VEAL, J Ross, Washington, D C	259
WARREN, SHIELDS, Boston, Mass	882
WATSON, WILLIAM L, New York, N Y	86
WEEDER, S DANA, Philadelphia, Pa	184
WEEKS, CARNES, New York, N Y	251
WEST, JOHN PETTER, New York, N Y	19
WHEELOCK, MARK C, Boston, Mass	882
WILLIER, B H, Baltimore, Md	598
WOMACK, NATHAN A, St Louis, Mo	34
WYLIE, ROBERT H, New York, N Y	127
YOUNG, FORREST, Rochester, N Y	445
ZEMAN, ERWIN, LT M C, Ft Lee	342



SYMPOSIUM ON TUMORS



INVASION OF THE BONY PELVIS BY CARCINOMA OF THE CERVIX UTERI AS A CAUSE OF PATHOLOGIC CENTRAL DISLOCATION OF THE HIP

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IN A HUNTERIAN LECTURE, in 1923, C A Joll stressed the fact that squamous cell tumors have a strong tendency to give rise to secondary growths in the skeleton, and, in support of this contention, quoted examples in which the primary neoplasm was in the uterus, tongue, esophagus soft palate and penis. Carcinoma of the cervix uteri gives rise to metastatic deposits in bone less often than tumors of the corpus, which, according to Ewing, Willis, and other authors, form distant metastases in 5 per cent, or more, of fatal cases. Turner and Jaffe (1940) found eight cases with skeletal metastases in a series of 99 patients with cervical growths, but this must be regarded as an unusually high number. In postmortem reports on large series of cases, such as those compiled by MacCormack (1909), and Albers-Schonberg (1893), skeletal deposits are estimated to occur in less than one per cent. We have not ourselves observed a case. As a source of skeletal metastases carcinoma of the cervix uteri may be regarded as of minor importance.

During recent years, the invasive powers of cancer in closed cavities have received special emphasis. These are well demonstrated by the tumors at the thoracic inlet, first described by Pancoast, which, by involving the structures at the root of the neck in a neoplastic mass give rise to the syndrome which bears his name. A striking and constant roentgenologic feature of these growths is that they invade the upper ribs and occasionally the vertebral column. The object of the present communication is to draw attention to the effects of similar direct invasion of the pelvis in the late course of carcinoma of the cervix, of which little notice has been taken hitherto. This local destruction is not of uncommon occurrence, and its consequences may contribute largely to the clinical picture.

It has been stated by Warren, Harris and Graves (1936) that carcinoma of the prostate invades the bones of the pelvis by extension along the perineural lymphatics, and Meigs and Jaffe (1939), and Auster and Sala (1940), have argued that carcinoma of the cervix may reach them in the same way. The experiments of Batson (1940) have shown, beyond doubt, that carcinoma of the prostate is distributed to the bones of the spine and pelvis by the venous system. It seems, equally beyond doubt, that carcinoma of the cervix attacks the pelvic wall as the final stage in a continuous lateral spread. Victor Bonney has repeatedly stressed the importance of the nodes high up in the obturator fossa, in the lymphatic spread of carcinoma of the cervix, and it is in their neighborhood that skeletal invasion by direct extension begins and reaches its maximum. The mass of nodes, when it attains large size, may be felt *per vaginam*, and its outline may, occasionally, be seen in roentgenograms. The region of the acetabulum is most usually affected, but local extension in other directions may destroy other portions of the pelvis.

In the ultimate stage, also, pathologic dislocation of the hip, or *protrusio acetabuli*, may take place, and this, in our experience, is the most common cause of this rather rare event. The fact that it may occur in this way is insufficiently recognized. Illingworth and Dick (1941), for example, state that pathologic dislocation of the hip is always of the dorsal variety, while Watson-Jones (1940) makes no mention of malignant disease as a factor in its production. Vacchelli, quoted by Watson-Jones (1926), records the occurrence of central dislocation in tuberculous disease of the hip, but we have not found mention of it in the present connection. In the cases of which notes are appended, central dislocation due to destruction of bone in the region of the acetabulum is shown at various stages of its development. It is perhaps relevant to note that over the considerable period in which these cases were observed the only instance of traumatic dislocation of the hip of any variety, that came to our notice was of central dislocation in association with *fragilitas ossium*.

Pain in these cases is often extremely severe, and appears to be due to implication of the sacrococcygeal plexus or the obturator nerve in the malignant process, though in advanced cases the lesion in the bone must make a large contribution. While it must be admitted that the grossest degrees of bony destruction are not very frequently seen, it seems equally true that this is only because so many patients die from sepsis, hemorrhage or uremia before these lesions have had time to develop, and that routine roentgenologic examination of the pelvis in cases of inoperable carcinoma of the cervix would reveal it in its earlier stages much more frequently than is appreciated.

CASE REPORTS

Case 1—The patient was 47 years of age. Her illness began with vaginal bleeding two and one-half years before admission. She was treated with radium followed by total hysterectomy in June, 1933, and remained fairly well for a year. She then noticed several small lumps over the pubis, and had further radium treatment, which was re-

peated in October, 1934, and, again, in June, 1935. She fell and hurt her right hip, September 24, 1935, two days before her admission.

She was found to be in poor general condition. Several small masses were palpable above the pubes on each side of the midline. Movement at the right hip was slight, and extremely painful. She died eight days later.



FIG 1—Case 1. Roentgenogram of pelvis, showing the outline of a neoplastic mass in relation to the right acetabulum, invasion of the adjacent bone, and central dislocation of the hip.



FIG 2—Case 2. Roentgenogram of pelvis showing outline of neoplastic mass, decalcification in acetabular region, and impending central dislocation.



FIG 3—Case 3. Roentgenogram of pelvis, showing commencement of carcinomatous invasion.



FIG 4—Case 3. Roentgenogram of pelvis, showing gross degree of destruction, with impending central dislocation of the left hip.

In the roentgenogram of the pelvis (Fig 1) the outline of a neoplastic mass, in relation to the right acetabulum and obturator foramen, is clearly seen. There is decalcification and erosion of the bone in the region of the acetabulum and the ischium, with central dislocation of the femoral head.

Case 2—The patient, age 61, was admitted, July 11, 1936, complaining of vaginal bleeding for nine months and urinary incontinence for three days. She had been in severe pain of a "bearing-down" character for a month. She was found to have an indurated ulcer replacing the cervix and involving the fornices and the vaginal walls, and infiltrating the tissues on the right side of the pelvis. Her pain became agonizing, with radiation along the distribution of the obturator nerve. She died August 11, 1936.

In the roentgenogram (Fig 2) the outline of the tumorous mass is again apparent. The right acetabular region is invaded and decalcification has proceeded to a considerable

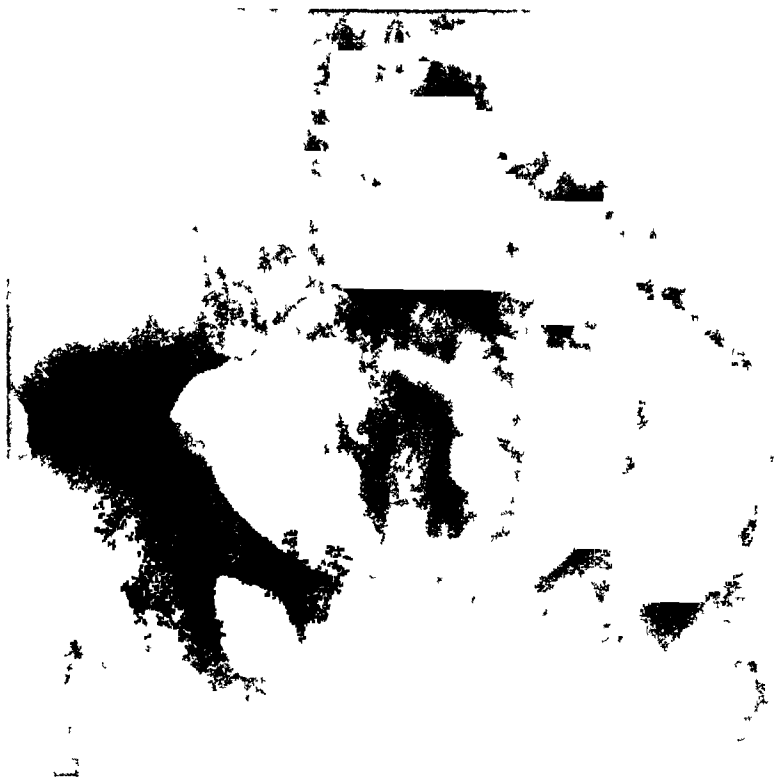


FIG. 5—Case 4. Roentgenogram of pelvis showing pathologic fracture in the region of the acetabulum.



FIG. 6—Case 4. Photograph of gross specimen obtained at autopsy showing tumor tissue invading the base of the acetabulum.

degree It is evident that a comparatively small force applied to the trochanter would produce central dislocation of the femur

Case 3—The patient, age 39, was admitted, December 7, 1939, complaining of swelling of the left leg for six weeks A carcinoma of the cervix was treated with radium in 1935, followed by three doses of deep roentgenotherapy She had been well until the leg began to swell No mass could be felt in the pelvis One month later, the pain had become severe, commencing in the left sacrosciatic foramen and radiating to the foot A tender, diffuse mass could be felt *per vaginam*, high on the left side The cervix appeared healthy, and the uterus was small and mobile A roentgenogram taken at this time (Fig 3) shows commencing invasion of the ileum Much relief was obtained by endothelial injection of alcohol, but for a short time only, and this was repeated on several occasions The patient's condition gradually became worse, with steady enlargement of the neoplastic mass and progressive destruction of the pelvic wall The pain in the leg was excruciating at times, and was relieved only by division of the spinothalamic tract and, finally, April 4, 1940, by partial chordotomy The patient died, June 21, 1940

The last roentgenograms of the pelvis, which it was possible to secure (Fig 4), was taken five weeks before death, and shows a gross degree of destruction, with impending central dislocation This actually took place three weeks later, when the patient turned in bed

Case 4—The patient, age 61, was admitted, February 7, 1941, complaining of pain in the back for six months She had had deep roentgenotherapy for carcinoma of the cervix in October, 1940 There was a large neoplastic ulcer in the region of the cervix, with palpable extension in the right side of the pelvis She complained of severe pain in the right hip and leg from shortly after her admission until her death, which took place June 17, 1941 No injury had occurred

A roentgenogram (Fig 5), obtained postmortem, shows a pathologic fracture in the region of the acetabulum The opacity in the lumbar vertebrae is not a metastasis

At autopsy, tumor tissue was found to infiltrate the whole inner membrane of the pelvis, especially on the right side, and to involve the region of the right acetabulum, where the bone (Fig 6) was infiltrated with whitish tumor tissue

REFERENCES

- ¹ Albers-Schonberg, H Beitrag zur Statistik des Carcinoma Uteri Jahresh d Hamburgischen Staatskrankenanstalten, 4, 62, 1893
- ² Auster, L S, and Sala, A M Causes of Death in Cancer of the Cervix Uteri Surg, Gynec, and Obstet, 71, 2, 1940
- ³ Batson, O V The Function of the Vertebral Veins and their Role in the Spread of Metastases ANNALS OF SURGERY, 112, 138, 1940
- ⁴ Graves, R C, Warlen, S, and Harris, P N Trans Am Genito-Urin Surg, 29, 179, 1936, Arch Path, 22, 139, 1936
- ⁵ Illingworth, C F W, and Dick, B M Textbook of Surgical Pathology London, J & A Churchill, 1941
- ⁶ Joll, C A Metastatic Tumours of Bone Brit Jour Surg, 11, 38, 1923
- ⁷ MacCormack, H Malignant Disease of the Cervix Uteria Arch Middlesex Hosp, 15, 20, 1909
- ⁸ Meigs, J V, and Jaffe, H L Ureteral and Renal Complications of Carcinoma of the Cervix Surg, Gynec, and Obstet 69, 262, 1939
- ⁹ Morris, J H, and Harken D E The Superior Pulmonary Sulcus Tumor of Fan-coast in Relation to Hare's Syndrome ANNALS OF SURGERY, 112, 1, 1940
- ¹⁰ Turner and Jaffe Metastatic Neoplasms Am Jour Roentgenol, 43, 483, 1940
- ¹¹ Watson-Jones, R Fractures and Other Bone and Joint Injuries Edinburgh E & S Livingstone, 1940
- Idem* Spontaneous Dislocation of the Hip Brit Jour Surg, 14, 36, 1926

UROLOGIC COMPLICATIONS OF CANCER OF THE RECTUM*

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A STUDY of the records of patients suffering from cancer of the rectum reveals an unusually high incidence of complications affecting the urinary system. While many of these become evident only after operation, they are frequently present before. It is difficult, however, to evaluate these pre-operative urinary symptoms in many instances, because, in taking the history, there has been no definite attempt to elicit them. Kickham and Bruce⁶ found that 30.4 per cent of males and 36.7 per cent of females, in the early operable group, had urinary symptoms while in late or inoperable instances of the disease, 60.7 per cent of males and 46.6 per cent of females had disturbances of urination. We have scrutinized the records of 93 patients in four different hospitals and find that 50 per cent of them presented symptoms of urinary difficulty upon admission. In a large number of the remaining 50 per cent, there was no record of interrogation in this regard. This group of 93 patients comprised 60 males and 33 females, the average age was 58, the youngest being 23 and the oldest 78. Thus, the greater part of them were in the age-group when such symptoms as nocturia, difficulty in urination, alterations in the urinary stream, pain and burning upon urination and other symptoms of cystitis are commonly present. A certain number of the males have latent obstruction at the neck of the bladder from various causes, the commonest of which is benign hypertrophy of the prostate and prostatitis. Engel² found this to be true in 5 per cent of 190 men operated upon at the Cleveland Clinic, and Fell³ states that 12 out of 64 (18 per cent) of his group gave a prostatic history. In the group making up our study, the prostate was said to be enlarged in 29 per cent of those in whom the condition of the gland was noted, but in 50 per cent of the records the prostate was not mentioned, and the residual urine was estimated in only two. In the females, the condition of the anterior vaginal wall and the position of the bladder were not especially noted in 21 out of 33, in the remaining 12, marked cystocele and prolapse, causing pronounced difficulty in urination, was found in three.

More careful questioning and examination probably would have revealed a greater number of persons in this group who were potential candidates for urinary complications, if they actually were not having symptoms at the time. It seems that the discovery of such a serious disease as cancer of the rectum overshadows these other conditions, both in the mind of the patient and in

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the attention of the physician. In addition to these ordinary causes of urinary symptoms, the neoplasm of the rectum is, itself, a frequent cause, and with the advance of the disease the symptoms become more numerous and more marked. The close anatomic relationship of the bowel and the urinary passages, with the tendency to penetration of the coats of the bowel, increasing its permeability to a septic content and causing adherence of structures are factors in the etiology of these symptoms. There may be external pressure of a tumor, causing distortion of the ureter, bladder, or urethra, or variable degrees of narrowing up to actual obstruction. Ulcerating growths on the anterior wall of the lower half of the rectum are most liable to cause trouble. In Kickham and Bruce's⁶ series there was evidence of extravesical pressure in 37.5 per cent, and actual bladder involvement in 25 per cent. In our study, since cystoscopy was undertaken in only two instances, we are unable to state the percentage of cases in which external pressure with distortion or obstruction was present. However, there was definite attachment to the bladder in four, the prostate in nine, urethra in one, and the vagina in three. The location of the neoplasm is shown in Table I.

TABLE I
LOCATION OF NEOPLASM

	No. of Cases
Upper rectum	48
Lower rectum	42
Not stated	3
Anterior wall	26
Posterior wall	17
Not stated	50
Attached to	
Bladder	4
Prostate	9
Urethra	1
Vagina	3
Sacrum	1

Examination of the urine before operation revealed pus cells in 38 per cent. Red blood cells were present in variable amounts in 16 per cent, there was one instance of frank hematuria. Bacteria were present in 12, of these only one was cultured, a streptococcus being recovered.

TABLE II
URINE BEFORE OPERATION

White Blood Cells	
Under 10 to H. D. F.	57
Over 10 to H. D. F. (10 to loaded)	36
Red Blood Cells	
Present in	15
Bacteria	12
Cultures—streptococci	1

We feel that a more detailed history would have revealed an even higher incidence of urinary symptoms upon admission and that examination of the

urinary tract with special emphasis on the detection of latent obstruction of the bladder neck should be undertaken in every case. Since symptoms of obstruction may later be due to operative nerve injury, it is desirable to have ruled out, and corrected, any other cause of obstruction in order to avoid confusion and misdirected treatment. The more frequent use of the cystoscope preoperatively, and routine urine cultures give information that helps to prevent the complications that occur after operation. The preoperative use of urinary antiseptics and irrigation of the bladder has the combined advantage of accustoming the urethra to the passage of a catheter and lessening the degree of infection. During the time of preparation for radical removal of the rectum, surgical correction of bladder-neck obstruction might be undertaken, and attention given to infected, sagging bladders in the female. The practicability of preliminary prostatic surgery is stressed by Kickham and Bruce⁶ who emphasize the fact that "A previously compensated bladder in the presence of obstruction may be precipitated into complete retention by weakening of the detrusor" (by interference with vesicle innervation). Engel² also recommends relief of obstruction at the bladder neck first in patients who have dysuria and are approaching operation for cancer of the rectum.

TABLE III

IRRIGATORIAL URINARY SYMPTOMS 93 PATIENTS

No symptoms related to the urinary tract mentioned in the history in	47
Symptoms present in	46
Nocturia	21
Dysuria	13
Pain and frequency	10
Burning on urination	5
Difficulty starting stream	3
Slow starting stream	2
Small stream	2
Urgency	2
Discomfort in bladder	1
Hematuria	1

EXAMINATION

Prostate enlarged	9
Not enlarged	22
Not mentioned	29
Residual urine estimated in	2
Cystocele	3
Cystocele and prolapse noted as not present in	9
Not mentioned in	21
Cystoscopy	2
Blood chemistry	23
Renal function dye excretion	60

Postoperative Complications—The frequency of serious urinary difficulty after radical removal of the rectum has often been remarked, but is not generally appreciated. Hill, Barnes, and Courville⁷ state that in answer to a questionnaire sent out by them, 32 surgeons reported an instance of 50 per cent of vesical dysfunction following resection, 20 reported it in two-thirds,

or more, of their patients and seven reported its occurrence in 100 per cent of their cases. Kickham and Bruce quote Cattell as saying that over 75 per cent present such complications and Whipple¹² says that "Frank urologic complications occurred in 50 per cent of his cases of radical resection." In the present study, the incidence was 64 per cent, complications occurring in 38 males and 18 females. The operations performed were of various types, and in 67 per cent spinal anesthesia was employed, the remainder being general, with one local.

TABLE IV

TYPE OF OPERATION

Operation in 87, no operation 5, radium 1	
Abdomino-perineal resection	
1 stage	35
2 stages	9
Posterior resection—Kraske	7
Colostomy posterior resection—Lockhart-Mummery	14
Hartman operation	2
Colostomy	15
Local excision	3
Perineo-abdominal resection	1
Resection and end-to-end anastomosis	1
Transfusions in	64

ANESTHESIA

Spinal	59
General	27
Local	1
Operations were performed by a number of surgeons—in four hospitals	

TABLE V

POSTOPERATIVE UROLOGIC COMPLICATIONS 64 PER CENT
Males 38, Females 18

Retention	56 (64%)
Cystitis	28 (33%)
Pyuria	30 (35%)
Pain burning distress	17 (19%)
Dysuria	2
Hematuria	2
Epididymitis	2
Frequency	1
Anuria	1
Incontinence	1
Atonic bladder	1
Pyelonephritis	1
Edema of penis and scrotum	1
*Neurogenic bladder	1

* (Male, age 48. Adenocarcinoma just inside anus. Abdominal Perineal Resection 1 stage, Spinal anesthesia Catheterized four months)

These complications following operation are due to one or all of four factors.

First, direct injury to the tract. This occurred in two instances in this group, one, an intentional partial resection of the urethra, the other, an unintentional injury to the urethra with subsequent perineal urinary fistula. Such accidents may be unavoidable in the difficult dissection that is sometimes

entailed, and the only precaution that can be taken is to identify the structures carefully. A great aid to this is the presence of a catheter in the urethra or the ureters, as the case may be, during operation. There is always considerable reaction in the base of the bladder and the urethra when close dissection is necessary, sections of the bladder wall show this in the form of ecchymosis, thrombosis of small vessels, and infiltration with inflammatory products after a few days.

Second, loss of the supports of the bladder in the destruction of the pelvic floor with postoperative sagging of the bladder into the large posterior dead space, which is always infected. This causes pooling of the urine in the hanging sac of the bladder which soon becomes infected in every case. Leich quotes Hochenegg and Heyrovski, who showed direct extension of bacteria into the intact bladder after operation. Postoperative packing of the posterior wound will help to prevent this, but the pack must be left long enough to permit the bladder to become fixed. Unless the pack is held in place by some sutures it quickly falls out and prolapse of the bladder occurs.

Third, the necessity for postoperative catheterization, with the almost inevitable infection that follows. Fell¹ states that 25 to 30 per cent of patients will void spontaneously, in this group, 32 per cent voided normally in the first 24 hours, 68 per cent were catheterized, intermittently in 27 per cent and by a retention catheter in 41 per cent.

TABLE VI

INCIDENCE OF CATHETERIZATION—68 PER CENT

Voided normally in first 24 hours	27 (32%)
Intermittent catheterization in	24 (27%)
Duration	
Average	10 days
Longest	32 days
Retention catheter in	36 (41%)
Duration	
Average	15 days
Longest	120 days

In one hospital, it is routine procedure to place a retention catheter in all cases, so that in all of their patients retention must be said to have occurred. In four or five days the catheter is removed and the patient is stimulated to try to void, if unsuccessful the catheter is replaced. In another hospital, intermittent catheterization was employed twice as often as was a retention catheter, and in the two other hospitals the two methods were employed about equally. It is to be remarked that postoperative orders in regard to catheterization were very variable, and in only one of the institutions were there definite and specific orders as to who was to catheterize, and as to when, and how it was to be done. Such orders as "If unable to void catheterize," "If distended catheterize," or "If in pain catheterize" were noted, and indicate a lack of appreciation of the damage that can be done to the bladder by overdistention and infection. This has been shown by Munio and Hahn⁸ in their study on tidal damage.

TABLE VII

Hospital	No of Cases	Voided 24 hrs	Retention Catheter	Intermittent Catheter	Cystitis	Pyuria
A	25	2	23	0	14	19
B	24	10	7	7	5	4
C	25	11	5	9	5	5
D	13	5	3	5	4	2

In hospital A, there were frequent examinations of the urine after operation, in the other hospitals, there were a large number in which this was not done, so that the incidence of pyuria and cystitis is undoubtedly higher

TABLE VIII

URINE AFTER OPERATION

No record of examination	47	Cultures	6
White blood cells		Streptococci, <i>B coli</i> , rods and chains, gram-	
Less than 10 to H P F	11	negative rods, cocci	
More than 10 to H P F	35	One man catheterized 34 days had but one urinal-	
(40-50-100-loaded)		ysis Another for 14 days until death had one	
Red blood cells	28	examination	
Bacteria	19		

It is needless to say that every time a catheter is passed, especially into a damaged bladder, the possibility of infection again presents itself, and the indwelling catheter should be employed only with continuous tidal drainage, with occasional periods of rest for the urethra Dukes¹ showed that pyuria appeared punctually in six to eight days in all women, and in 14 men, in whom a retention catheter was employed without tidal drainage In the majority, this lasted for several weeks and in some for months Two or three days before pus appeared, staphylococci were recovered in pure culture and a little later cultures showed mixed growths of *B coli* and staphylococci His cases were studied by daily microscopic examination of the urine and frequent cultures, in order to answer the question "Has the patient escaped urinary infection?" It is remarkable that in so large a number of the cases studied by us (47 out of 87), there was no record of urinalysis after operation Whipple¹² says that if adequate investigation of the urine were carried out in all cases, the incidence of cystitis after operation would be found to be 100 per cent

Dukes uses a form for the recording of the incidence of pus cells as follows

100,000	}	Pus 2 plus
10,000		
1,000	}	Pus 1 plus
100		
10	}	Pus
0		
	}	Excessive leukocytes
	}	Normal

The comparative merits of retention and intermittent catheterization has caused some debate Many authorities place an indwelling catheter in the

bladder before or at the end of the operation, and leave it in for from four to five days to two weeks. After this period, intermittent catheterization is persisted in until there is no longer any residual urine. Fell³ says that T. E. Jones has given up the use of a retention catheter and thinks that it is best to catheterize three or four times a day, having found that this plan leads to fewer complications. David also prefers intermittent catheterization, feeling that it causes less trauma to the urethra and is more comfortable for the patient.

Fourth, Injury to the Nerve Supply of the Bladder.—Why, out of a series of cases having the same type of operation, some will develop serious vesical

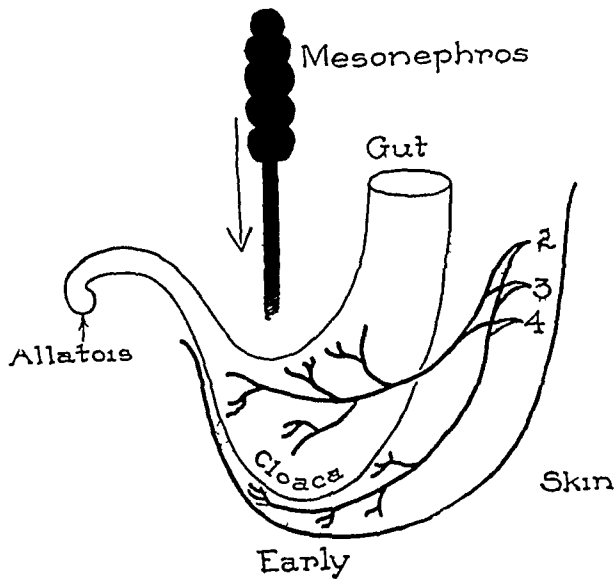


FIG. 1.—The cloaca and its nerve supply. (Redrawn from 'A Method of Anatomy' by J. C. Boileau Grant Williams and Wilkins Co. Publishers.)

disability and others will escape, has been an intriguing question. It must be a question of anatomy, probably of fascial barriers and cleavage planes.

Grant,⁴ in his *Method of Anatomy*, says that in lower forms the cloaca opens onto the skin surface through an opening guarded by a sphincter of striated muscle. In man, a septum of mesoderm, the urorectal septum divides the cloaca into an anterior and a posterior part, this also occurs to the cloacal sphincter, the anterior part becoming the transversus perinei, bulbospongiosus, ischiocavernosus, and the urogenital diaphragm, the posterior part becoming the sphincter ani externus. For these reasons, one nerve, the pudendal, a mixed nerve, supplies all of the muscles into which the cloacal sphincter divides as well as the skin about the orifice. The bladder and the rectum, for this reason, have a common nerve supply also, consisting of the pelvic splanchnic, which is parasympathetic, and most important, the hypogastric plexus, which is sympathetic, and the pudendal which is somatic. The pelvic splanchnic and the pudendal both arise from the second, third, and fourth

sacral segments, the pudendal is a mixed nerve which supplies voluntary muscle including the sphincter ani externus and the sphincter urethrae. The pelvic splanchnic, nervus erigens, is a mixed parasympathetic nerve, it supplies the involuntary muscles guarding the rectum and the bladder, the sphincter ani internus and the sphincter vesicae, as well as the detrusor muscle in the bladder wall. As it also supplies the arteries of the erectile

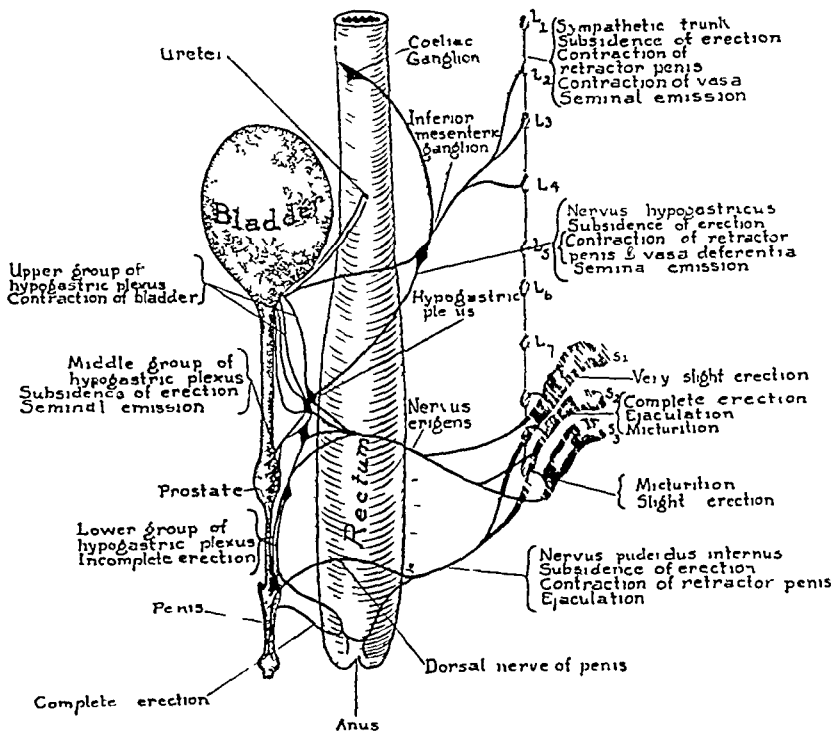


FIG. 2—Pelvic nerve supply in the cat. (Redrawn from 'Physiology of Micturition' by Lingworthy, Kolb and Lewis. Williams and Wilkins Co., Publishers.)

tissue of the penis and the clitoris, causing their relaxation and erection, it is called the nervus erigens. The afferent and the efferent fibers for the bladder are, therefore, in the paired pelvic splanchnic nerves, and for the urethra, in the paired pudendal nerves. The sympathetic fibers to the bladder travel by the mesenteric, hypogastric and pelvic plexuses. The sympathetic trunk passes down on the bodies of the vertebrae behind the common iliac artery to reach the pelvis, branches pass from this trunk to the intermesenteric plexus, which extends down to become the hypogastric plexus or presacral nerve. This nerve lies below the bifurcation of the aorta, in front of the left common iliac vein and the promontory of the sacrum, on each side branches descend in front of the sacrum as the right and left pelvic plexus and are joined by branches of the pelvic splanchnic.

The relations of the pelvic splanchnic are of much greater importance in relation to the subject under discussion. Giant⁴ says that they are most easily found by "passing two fingers down in front of the body of the sacrum and easing the rectum forward the fingers will occupy a little pouch which is bounded on each side by an areolar fold which contains the nervus erigens, and conducts it from the sacral foraminae to the side of the rectum." On

each side of the rectum, it joins the pelvic sympathetic of the same side and so becomes mixed sympathetic and parasympathetic. It forms a dense network, applied to the medial side of the vessels that limit the retroperic space posteriorly on each side, and is distributed to the pelvic viscera with these vessels. As it passes in from the paretics to the viscera the nerve is in three parts: a proximal one, related to the bladder; a middle one, which supplies the urethra and the sex glands; and a third, or distal one, which innervates the bowel (Langworthy, Kolb, and Lewis⁷ who also say that the autonomic system is purely motor and passes in as distinct units, the parasympathetics always lying lateral to the sympathetics).

Division or destruction of the parasympathetic fibers leads to an inability to empty the bladder; there is loss of normal tone and contraction, and the injury may be unilateral or bilateral. The bladder wall becomes hypertrophied and changes in the mucosa, due to infection, occur. Langworthy, Kolb, and Lewis believe that the sympathetic fibers have vasomotor and sexual functions in relation to the bladder and urethra, and that their activity is not necessary for normal micturition.

FIG 3

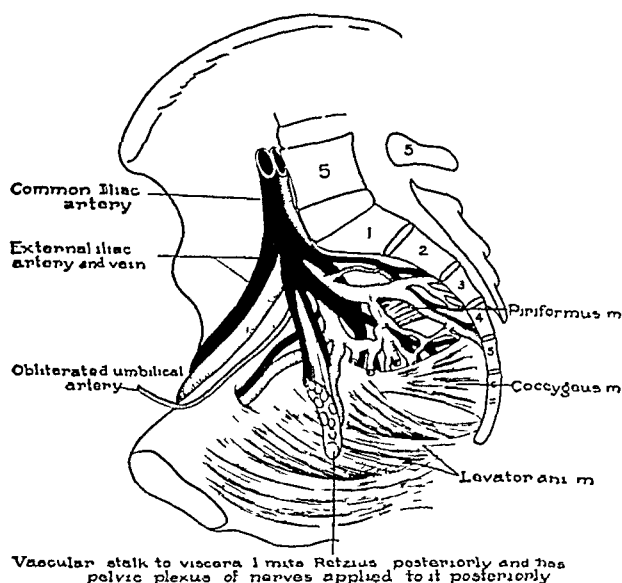
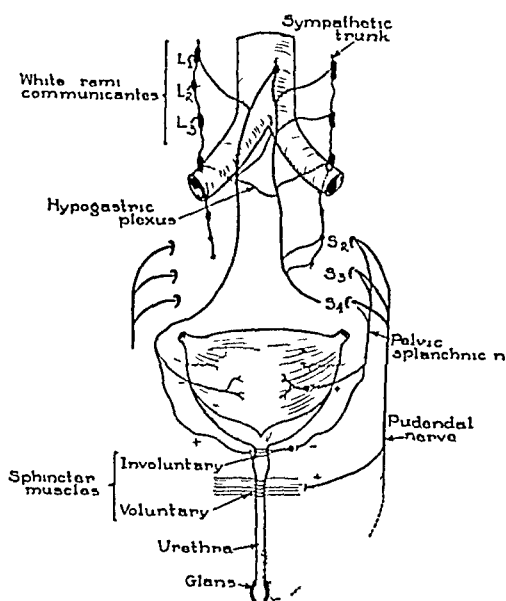


FIG 4

FIG 3—The nerve supply to the bladder and urethra (Redrawn from 'A Method of Anatomy' by J. C. Boileau Grant Williams and Wilkins Co., Publishers.)

FIG 4—Redrawn from 'A Method of Anatomy' by J. C. Boileau Grant Williams and Wilkins Co. Publishers

It would seem that the urinary dysfunction following excision of the rectum is usually due to injury to the parasympathetic nerve supply. It rarely occurs during the abdominal stage of the operation, and is rarely due to the encroachment of the tumor itself upon the nerve structures. It is

during the perineal or posterior resection that the injury usually occurs. It is at this stage that the pudendal nerve, also, is injured and, although it lies lateral to the usual line of incision, it may be injured by actual division or by traction. Its injury, or division, leads to incontinence, of which one instance occurred in this group. Mixed types of dysfunction can occur and are due to various degrees of injury to several of the nerve pathways.

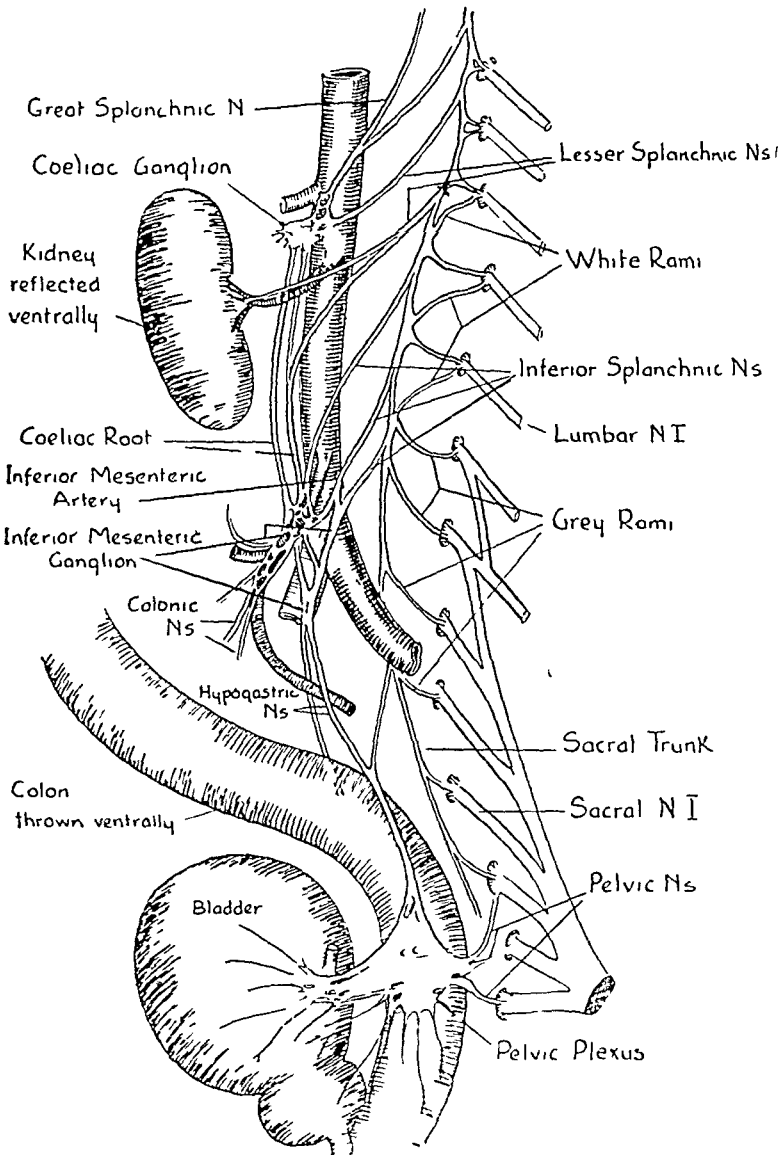


FIG 5—Arrangement of lumbar and sacral autonomic nerves in man (Tumble)

Descriptions of the pelvic fascia are difficult to understand, because it is not laid out in definite flat sheets, but covers the various pelvic viscera in diverging planes and angles. It is, however, probably due to a misconception of the distribution of the pelvic fascia that these injuries occur. There are four layers of fascia between the bladder and the rectum, according to Giant¹. A layer clothing the base of the bladder, a layer clothing the front of the rectum, and the two other layers that clothe the seminal vesicles and the vas in front and behind. It is in the layers on the posterior wall of the pelvis

that confusion exists. There are usually described in this area, two layers of fascia, one on the face of the sacrum and another clothing the posterior surface of the rectum. Dr. John Saunders, professor of anatomy of the University of California, believes that this is erroneous and teaches that the inner of these two layers, usually described as the fascia propria of the rectum, is in reality made up of two definite fascial sheets. He has demonstrated, to his satisfaction, in numerous dissections, and has applied the facts clinically in a number of cases of abdominoperineal resection. According to his teaching, the pelvic splanchnic nerves are carried in from the posterior pelvic wall to the sides of the rectum on the lateral aspect of this middle layer, forming the areolar leash previously described by Grant⁴. If the coccyx is excised one comes down on to a thick fascial layer that is made up of the endopelvic fascia and the periosteum. A vertical incision through this discloses a second layer that is usually considered to be the fascia propria of the rectum, but if a second vertical incision is very carefully made in this sheet, it will be found to be made up of two layers of fascia, with a definite cleavage plane between them. It is in this plane that the dissection should be carried laterally, in which event the pelvic splanchnic is pushed aside with the fascia and only those branches ending in the rectum are destroyed. When the dissection is carried laterally outside of this second, or middle layer, in the cleavage plane first encountered, the nerves are torn off the sacral foraminae before the fascia can be mobilized with resulting bladder paralysis of lesser or greater degree. When the dissection is made in the proper plane, the nerves can be seen passing toward the bladder, like a cable across the dead space. It is probable that failure to damage the nerve supply in all cases is simply due to the fact that one has inadvertently entered the proper cleavage plane.

In this series, there was one instance in which the diagnosis of neurogenic bladder was made, in several others, however, there was serious dysfunction with retention lasting for several weeks, and it has been said that whenever a patient is unable to void after five or six days there has probably been nerve damage. In the diagnosis of nerve injury, one must take into consideration the possibility that spinal anesthesia may be a factor. Pierson and Twomey⁹ discuss this aspect of the problem of retention and cite cases following spinal anesthesia for other operations in which pelvic nerve injury could not have occurred. There was one instance of anuria resulting in death seven days after operation. In this patient, a 48-year-old male, there was involvement of the membranous urethra, which was resected and the divided ends anastomosed, as a part of the second-stage of an abdominoperineal resection. Postoperative investigation, and autopsy, showed that there had been no operative injury to the urinary tract other than the urethral resection. In this case, the pathologist reported that the neoplasm was primary in the prostate, although preoperative biopsy had been diagnosed as epidermoid carcinoma of the rectum and careful urologic investigation had not altered

this opinion Kickham and Bruce⁶ state that sometimes the differential diagnosis between cancer of the prostate and carcinoma of the rectum is most difficult, and they have reported four cases of carcinoma of the prostate simulating primary malignant disease of the rectum. The cause of the anuria

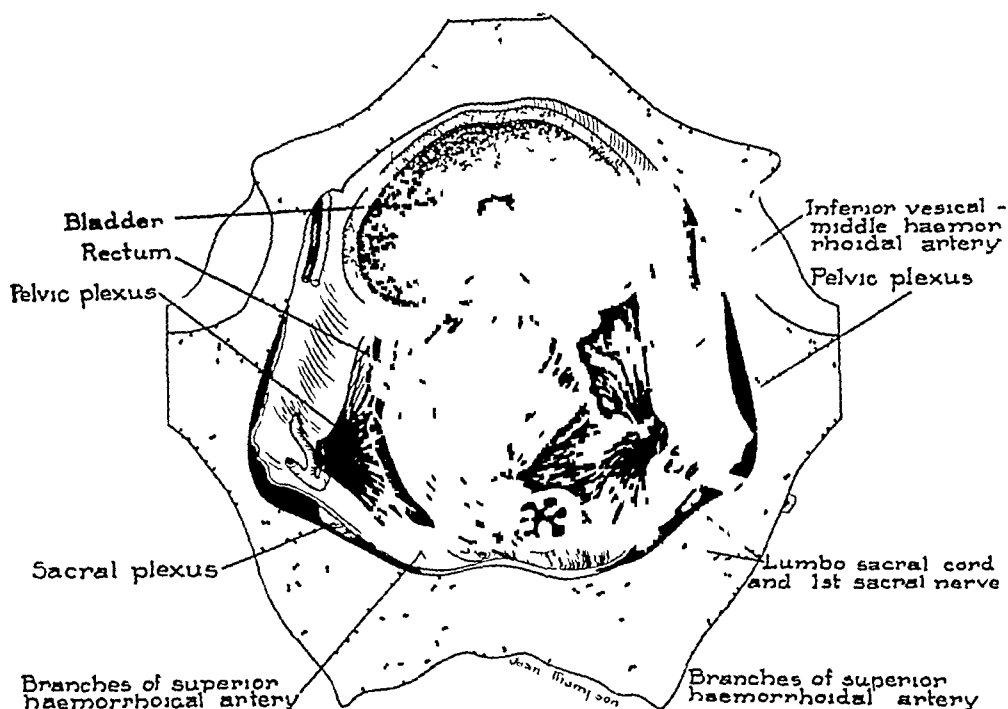


FIG 6—The pelvic plexus and fascia (Redrawn from Cunningham)

was not determined, although spinal anesthesia, transfusion and reflex influences were considered

CONCLUSIONS

(1) Symptoms relating to the urinary tract are found in a high percentage of patients having cancer of the rectum. These are not only due to the neoplasm itself but to the other causes of urinary difficulty, that often occur in patients of this age-group. More specific attention to these symptoms, preoperatively, is urged, especially in relation to bladder neck obstruction and incomplete emptying of the bladder. Investigation of the urine by microscopic study and culture should be undertaken in every case, both before and after operation.

(2) More serious attention to the operation of catheterization with attention to its details is imperative. The advisability of the routine use of retention catheters is questionable, as in one out of three patients normal urination will occur. If retention catheterization is employed, it should always be accompanied by tidal irrigation.

(3) Urinary dysfunction should not be considered a necessary part of total proctectomy. Preservation of the pelvic splanchnic distribution to the urinary and sexual apparatus should be the definite intention of the surgeon, and special attention should be given to the anatomy of the posterior pelvic fascial planes. An effort to prevent prolapse of the bladder into the posterior

wound should be made and every attention given to the prevention of its infection

REFERENCES

- ¹ Dukes, Cuthbert Urinary Infections after Excision of the Rectum Proc Roy Soc Med, **22**, 259, 1928
- ² Engel, William J Bladder Neck Obstruction Associated with Carcinoma of the Rectum Surg Clin North America, October, 1939
- ³ Fell, E H The Care of the Urinary Bladder Following Resection of the Rectum for Carcinoma Internat Clin, Series III, **48**, 1938
- ⁴ Grant, J C B A Method of Anatomy 2nd Ed, Baltimore, Williams and Wilkins Co, 1940
- ⁵ Hill, Malcolm R, Barnes, Roger W, and Couville, Cyril W Vesical Dysfunction Following Abdominoperineal Resection J A M A **109**, 1184-1188, 1937
- ⁶ Kickham, Charles J, and Bruce, Norman H Urologic Complications in Malignant Disease of the Rectum Jour Urol, **41**, 4, 1939
- ⁷ Langworthy O R, Kolb, L C and Lewis, L G Physiology of Micturition Baltimore, Williams and Wilkins Co, 1940
- ⁸ Munro, Donald Tidal Drainage of the Urinary Bladder New England Jour Med, **212**, 229-239, 1935
- ⁹ Pierson, Edward L, and Twomey, Charles F Neurologic Dysfunction of the Bladder Due to Spinal Anesthesia New England Jour Med, **223**, 171-174, 1940
- ¹⁰ Saunders, J B deC Personal communication
- ¹¹ Trumble, Hugh C The Plan of the Visceral Nerves in the Lumbar and Sacral Outflows of the Autonomic Nervous System Brit Jour Surg, **21**, 664, 1934
- ¹² Whipple, Allen O Complications Associated with Major Proctectomy ANNALS OF SURGERY, **96**, 916, 1932

PAGET'S DISEASE OF THE NIPPLE

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PAGET'S DISEASE of the nipple is not a common disease. Harrington,¹ in a review of 4,628 cases of carcinoma of the breasts, reports only 34 cases of Paget's disease, an incidence of 0.7 per cent. It is for this reason, perhaps, that the seriousness of an eczema of the nipple is not always appreciated.

In 1874, Sir James Paget² published an article titled "On Disease of the Mammary Areola Preceding Cancer of the Mammary Gland." He stated that "certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhous carcinoma of the mammary gland."

His classical description of the clinical features of the disease, in the 15 patients he had observed, is in part as follows: "The disease began as an eruption on the nipple and areola. In the majority it had the appearance of a florid, intensely red, raw surface, very finely granular, as if very nearly the whole thickness of the epidermis were removed, like the surface of a very acute diffuse eczema. From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish viscid exudation."

"It has happened in every case which I have been able to watch, cancer of the mammary gland has followed within, at the most, two years, and usually within one year. The formation of the cancer has not in any case taken place first in the diseased part of the skin. It has always been in the substance of the mammary gland, beneath or not far removed from the diseased skin, and always with a clear interval of apparently healthy tissue. In the cancers themselves, I have seen in these cases nothing peculiar. They have been various in form, some chronic, some acute, the majority following an average course, and all tending to the same end: recurring if removed, affecting lymph nodes and distant parts, showing nothing which might not be written in the ordinary history of cancer of the breast."

Because of the lack of a histopathologic description by Paget, there has been much confusion as to the true nature of the disease. Kilgore³ states that to-day a definite histologic picture is recognized, consisting of "epithelial hypertrophy, subepithelial round cell infiltration and Paget's cells." Paget cells, so-called, are large edematous cells in the epithelium vacuolated and with shrunken pyknotic nuclei. Muir^{4, 5} defines a Paget cell as a cancer cell growing within a healthy or at least nonneoplastic epithelium.

FIG 1

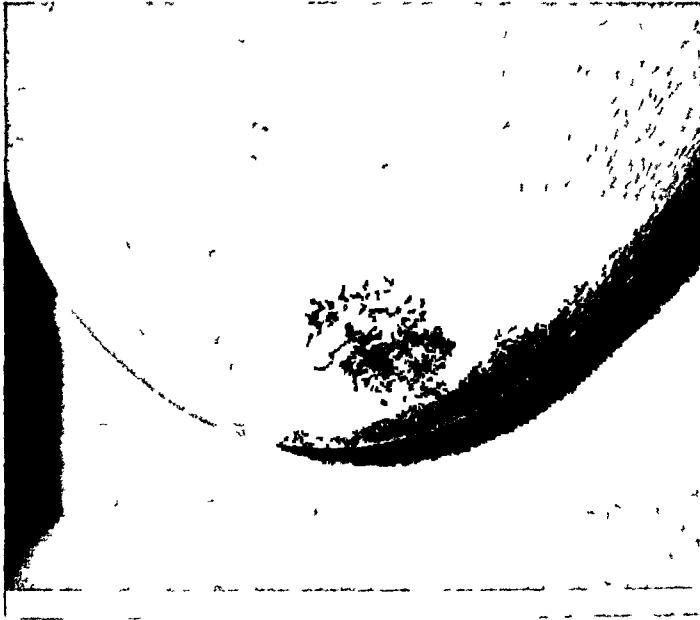


FIG 2

FIG 1—Case 1. Eczema of nipple and areola of two years duration. Radical mastectomy. Nodes not involved. Well nine years.

FIG 2—Case 1. Section through nipple. Many Paget cells are seen in the epidermis. (×275)

According to Caylor⁶ there are at the present four chief opinions regarding Paget's disease (1) That it is a dermatitis or eczema of the skin, (2) that it is a primary squamous cell epithelioma of the skin, (3) that it is a carcinoma developing from the lactiferous ducts in the nipple and the sudoriferous ducts of the skin, secondarily involving the skin and breast tissue, and (4) that it is a carcinoma beginning deep in the breast and growing up along the ducts of the nipple and finally invading the skin

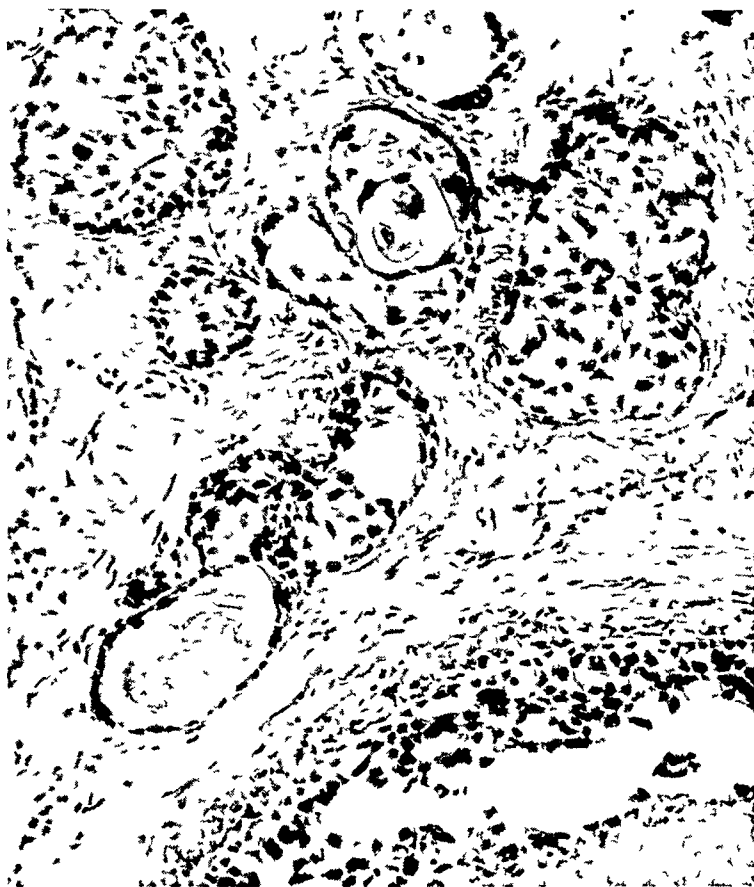


FIG. 3—Case 1 Section through breast showing intraduct carcinoma (×240)

Cheatle^{7, 8} feels that the classic signs that Paget described are caused by more than one condition and that it is not correct to limit the diagnosis of Paget's disease of the nipple to those states in which "Paget cells" are present

Muir believes that Paget's disease occurs only when intraduct carcinoma is present in the upper portions of the ducts in the nipple, and is due to the spread of the cancer cells from ducts to the epidermis by the intra-epithelial route

Weiner⁹ has published an excellent chronologic resumé of the more important literature on Paget's disease of the nipple. He was particularly interested in the extramammary form, and suggests that Paget's disease of the skin is the intra-epidermal metastasis from an underlying carcinoma of the apocrine sweat glands

Ewing¹⁰ states that "Paget's disease is a specific, chronic, progressive disease of the mammary nipple and adjoining skin, which is closely related

to, and almost invariably followed by, carcinoma. It is probably to be interpreted as a precancerous affection at first, limited to the epidermis and the gland ducts, but later becomes true carcinoma. The writer's conclusions regarding the nature of Paget's disease are influenced by clinical characters as well as histologic studies, which indicate that there are two clinical varieties. One finds a typical group of cases in which there is no definite tumor of the breast but a slowly progressive eczematous lesion affecting the epidermis about the nipple, not extending deeply into the ducts but spreading widely over

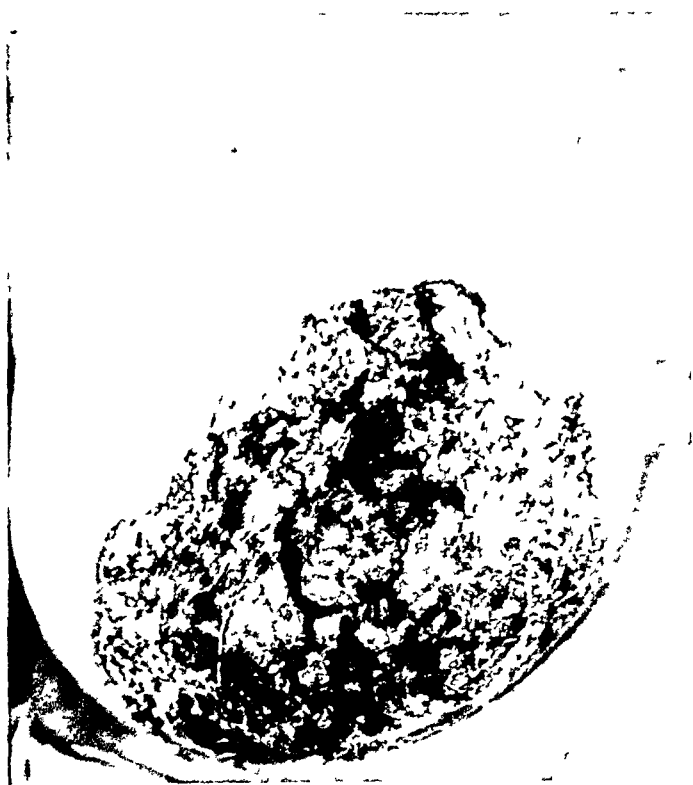


FIG. 4.—Case 2. Eczema of nipple and surrounding skin of one year's duration. Radical mastectomy. Nodes not involved.

the skin, with a favorable prognosis under treatment. Contrasted with these cases are others in which, from the first, there is a carcinoma of ducts or parenchyma, a limited involvement of skin, a diffuse invasion of breast, an unfavorable prognosis, and often a rapid course. It is difficult to accept the conclusion that these two maladies are identical in nature, differing merely in grade of malignancy, but histologic studies show that the lesions are very similar."

It is not the object of this report to enter into the controversy concerning Paget's disease of the nipple. We wish to report our experience with the disease and to emphasize the observation of Paget, namely, that most cases of chronic eczema of the nipple are closely associated with a true carcinoma of the breast.

We have reviewed the records of 20 cases of Paget's disease of the nipple. Through the courtesy of the Surgical Department of St. Luke's

Hospital we have been permitted to study 12 cases in their records. These patients were treated over a period of approximately 23 years (January, 1918–May, 1941), and eight were treated at the New York Hospital over a period of about nine years (September, 1932–May, 1941). The diagnosis in each case was based on the presence of an eczema or excoriation of the nipple which, on histologic section, showed epithelial hypertrophy, sub-epithelial round cell infiltration and Paget's cells.

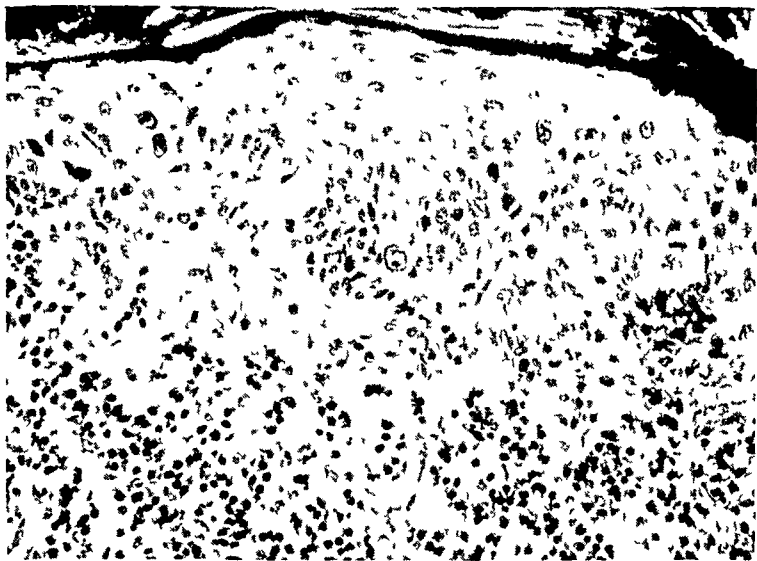


FIG. 5—Case 2. Section through skin. Shows direct invasion of epidermis by carcinoma cells. Only a few Paget cells in this section. (×280).

As suggested by Ewing, these cases are readily divided into two clinical groups. In the first group (Table I) of 13 cases, all but two of whom were over 50 years of age, the chief complaint of each patient was an eczema of the nipple, usually of long duration. In only three instances was the lesion of the nipple present for less than one year. Section of the breasts, after removal, revealed a definite tumor in eight of the 13 cases, and in three of the eight there were axillary metastases. Of the three patients with axillary metastases, one died six months, and another four years, after operation, the

TABLE I

GROUP I—PAGET'S DISEASE OF THE NIPPLE—CHIEF COMPLAINT ECZEMA OF NIPPLE

Case No	Age	Duration of Eczema	Breast Tumor	Mastectomy	Node Involvement	Result
1	74	6 yrs	No	Simple	Not removed	Well—2 mos
2	59	5 yrs	Yes	Radical	Yes	Died—4 yrs
3	60	4 yrs	No	Radical	No	Well—17 yrs
4	55	4 yrs	Yes	Radical	Yes	Died—6 mos
5	62	2 yrs	Yes	Radical	No	Well—9 yrs
6	57	18 mos	No	Simple	Not removed	Well—15 yrs
7	60	15 mos	Yes	Radical	No	Well—3 yrs
8	50	1 yr	Yes	Radical	No	Well—1 mo
9	67	1 yr	No	Radical	No	Well—2 yrs
10	64	1 yr	Yes	Radical	Yes	Well—1 yr
11	52	8 mos	Yes	Radical	No	Well—10 yrs
12	41	3 mos	No	Simple	Not removed	Well—4 yrs
13	47	2 mos	Yes	Radical	No	Well—3 yrs

third was subjected to operation only one year ago, and is alive and well, without evidence of recurrence. The remaining ten patients are alive and well, two, for more than 15 years, one, ten years, one, nine years, three for three years, and three operated upon within the past year.

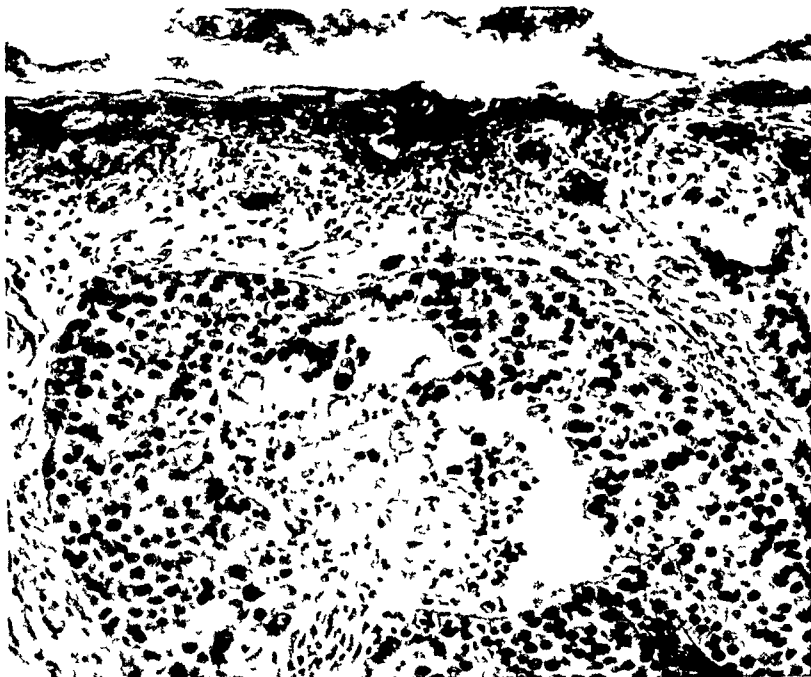


FIG. 6—Case 2. Section through breast. Shows a duct cell type carcinoma.

This group of 13 cases emphasizes the close relationship between chronic lesions of the nipple and carcinoma of the breast. It also suggests that carcinoma of nipple origin is slow to metastasize to the axillary lymph nodes and, therefore, forms a favorable group with proper treatment. We agree with Cohn¹¹ that all lesions of the nipple which do not quickly respond to simple treatment should be subjected to a biopsy which includes a good section of the underlying breast tissue, and if the histologic picture is that of Paget's disease a radical mastectomy should be performed.

In the second group of seven cases (Table II) all the patients were aware of a tumor of the breast at the time they sought medical advice, and only two complained of an associated eczema of the nipple. In fact the nipple lesions were so inconspicuous that in not a single instance was the clinical diagnosis of Paget's disease made. Histologic studies of the nipples, however, revealed changes similar to those of the first group. The second group is also distinct from the first in that the symptoms were of relatively short duration, the average being four months. Four of these patients are known to have died of their carcinomata within three years after operation, one has been alive for one year but has a local recurrence, and the result in the other two is not known.

TABLE II

GROUP II—PAGET'S DISEASE OF THE NIPPLE—CHIEF COMPLAINT BREAST TUMOR

Case No	Age	Duration of Tumor	Secondary Nipple Changes	Mastectomy	Node Involvement	Result
1	46	9 mos	Yes	Radical	No	Died—3 yrs
2	44	6 mos	Yes	Radical	No	Unknown
3	50	6 mos	Yes	Radical	Yes	Died—6 mos
4	38	3 mos	Yes	Radical	Yes	Died—2 yrs
5	40	2 mos	Yes	Radical	Yes	Died—2 yrs
6	50	1 mo	Yes	Radical	Yes	Recurrence—1 yr
7	62	1 mo	Yes	Radical	Yes	Unknown

CONCLUSIONS

From the clinical point of view there appear to be two groups of cases in which nipple changes characteristic of Paget's disease are noted (1) Those presenting an eczema of long standing, which may or may not be associated with a definite tumor in the breast, and in whom the prognosis is good with early surgical treatment, (2) those who, from the first, apparently have a carcinoma of the breast with secondary invasion of the nipple and in whom the prognosis is poor. Metastasis occurs in both groups, more frequently in the second than in the first.

The close relationship between chronic eczematoid lesions of the nipple and carcinoma of the breast makes it imperative that early and adequate biopsy be made of every chronic nipple lesion. If a diagnosis of Paget's disease is made, regardless of whether or not a definite tumor can be demonstrated in the breast, the patient should be subjected to a radical mastectomy.

REFERENCES

- ¹ Harrington, S. W. Unilateral and Bilateral Carcinoma of the Breast (Including Paget's Disease) Results 3, 5, 10, 15, and 20 Years After Operation. *Minnesota Med*, 21, 1-8, January, 1938.
- ² Paget, J. On Disease of the Mammary Areola Preceding Cancer of the Mammary Gland. *Med. Class*, 1, 75-78, September, 1936 (reprint).
- ³ Kilgore, A. R. Paget's Disease of the Nipple. *Arch. Surg*, 3, 324-335, 1921.
- ⁴ Muir, R. Paget's Disease of the Nipple. *Brit. Jour. Surg*, 22, 728-739, 1935.
- ⁵ Muir, R. Further Observations on Paget's Disease. *Jour. Path. and Bact*, 49, 299-312, September, 1939.
- ⁶ Caylor, H. D. Paget's Disease of the Nipple. *Surg. Clin. North America*, 9, 951-956, 1929.
- ⁷ Cheatle, L. Paget's Disease of the Nipple. *Lancet*, 2, 1462-1463, December 19, 1936.
- ⁸ Cheatle, L. Paget's Disease of the Nipple. *Surg., Gynec., and Obstet*, 66, 525-526, 1938.
- ⁹ Weiner, H. A. Paget's Disease of the Skin and Its Relation to Carcinoma of the Apocrine Sweat Glands. *Am. Jour. Cancer*, 31, 373-403, 1937.
- ¹⁰ Ewing, James. *Neoplastic Diseases*, 4th ed., Philadelphia, W. B. Saunders Co., 1940.
- ¹¹ Cohn, L. H. Paget's Disease of the Nipple, with Special Consideration of Biopsy and Preoperative Irradiation. *Arch. Surg*, 34, 201-229, February, 1937.

HEMANGIOPERICYTOMA

A VASCULAR TUMOR FEATURING ZIMMERMANN'S PERICYTES

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IN A RECENT COMMUNICATION, the writers demonstrated by the method of tissue culture that the epithelioid cell of the glomus tumor is derived from Zimmermann's pericyte. This is a contractile cell with long processes which wraps itself about capillaries and serves to change the caliber of their lumens. Zimmermann, and others, have suggested that these pericytes are modified smooth muscle cells. The glomus tumor is a complex organoid neoplasm furnished with many axis cylinders, which reproduces in caricature the normal neuromyo-arterial glomus. There occur, however, tumors composed of capillary blood vessels with one or more layers of rounded cells arranged about them, which cannot be called glomus tumors because they lack the organoid features of those encapsulated complex neoplasms, yet differ from simple capillary hemangiomata because of the presence of their perivascular cells. We believe that these cells are pericytes and that these tumors should be distinguished by a specific name and suggest "hemangiopericytoma" as properly descriptive.

In the past, one gathers that such tumors have generally been called hemangio-endotheliomata on the assumption that only the prolific and versatile vascular endothelia could give rise to these rounded perivascular cells. We have never agreed with this opinion but had no alternative suggestion for their origin until we learned about pericytes from the writings of Zimmermann and observed how greatly they differed from endothelia when grown *in vitro*. There are, indeed, vascular neoplasms that may properly be called hemangio-endotheliomata. These are malignant tumors of capillaries featuring the growth of neoplastic endothelia, which in addition to heaping up inside the lumen may invade the wall and proliferate outside but these tumors are very different from hemangiopericytomata in which the endothelia never differ from the appearance of normal endothelial cells.

It is probable also that Schmidt (1937) has included one or possibly two cases of hemangiopericytoma in a group of vascular tumors which, following the suggestion of Oisós (1934), he chooses to call gemmangiomata. Oisós revived the hypothesis of R. Meyer that blood vessels and blood cells are all derived from embryonal pluripotent cells called angioplasts. He then proceeded to describe a number of vascular tumors, some composed in part of capillaries and in part of immature endothelial sprouts without lumens and others

much more complex with both capillaries and immature red and white blood cells Oisós also included tumors which did not seem primarily vascular at all, and in attempting to follow his lead Schmidt included under the name gemmangioma tumors which seem to us to be xanthoma and liposarcoma If Oisós had restricted the term gemmangioma to tumors composed of immature capillary sprouts, the term might be acceptable But since he has chosen to make it cover a heterogeneous variety of tumors which Schmidt has further enlarged, we believe that only confusion will follow any attempt to perpetuate the term

In our collection of 691 blood vessel tumors, we find nine cases to which the name hemangiopericytoma may be applied in addition to 38 glomus tumors for which the term might also be used This group of nine tumors is an interesting one because it includes cases showing most of the biologic features exhibited by other vascular tumors including locally persistent aggressive infiltrative growth in one instance and distant metastasis resulting in death in another In another crucial case, the probable relationship between pericyte and smooth muscle cell is strongly suggested because the cells arranged about the tumor vessels vary all the way from the usual rounded pericyte through an indeterminate phase of spindle shapes to a fully differentiated cell with myofibrils

The first four cases are all alike histologically, and demonstrate the usual appearance of this neoplasm

CASE REPORTS

Case 1—A male, age 45, had a tumor the size of a dressmaker's pin on the dorsal surface of the left ring finger It looked like a nonpigmented mole If struck it would bleed and become sore, otherwise it gave no trouble After an attempt to destroy it by electrocauterization failed, it was excised Three years later there was no evidence of recurrence (Case made available by Dr F A Patterson of Norwalk, Conn, and Dr Gray Twombly, New York)

Case 2—When this female infant was born, a small "birthmark" was noted in the skin at the outer margin of the breast It was excised at the age of six months The case was not followed (Case made available by Dr Howard Meyer, Hackensack Hospital, N J)

Case 3—When this female infant was born, there was a small red spot in the skin of the parietal region At age three months it had reached a diameter of 1 cm and was excised It was quite vascular but did not extend beneath the galea The case was not followed (Case made available by Dr A O Severance, San Antonio, Texas)

Case 4—Age and sex unknown Five months before, a blow was received on the shoulder and another one two months later Following this a lump appeared in the skin and grew larger It was tender, attached to the skin but otherwise freely movable It was excised and the case was not followed (Case made available by Dr H Meyer Hackensack Hospital, N J)

Pathologic Characteristics—All of these tumors are made up of groups of endothelial-lined tubes filled with erythrocytes and of endothelial sprouts without lumens Both are supported by delicate reticulin fibers outside of which are arranged the rounded pericytes These sometimes form a single layer or they may be in such numbers that all of the space between neighboring vessels may be filled with them Some vessels may have no pericytes No elastic fibers are formed Like ordinary capillary hemangiomata,

the groups of tumor vessels infiltrate the skin and sometimes the subcutaneous fat to a limited degree (Fig 1)

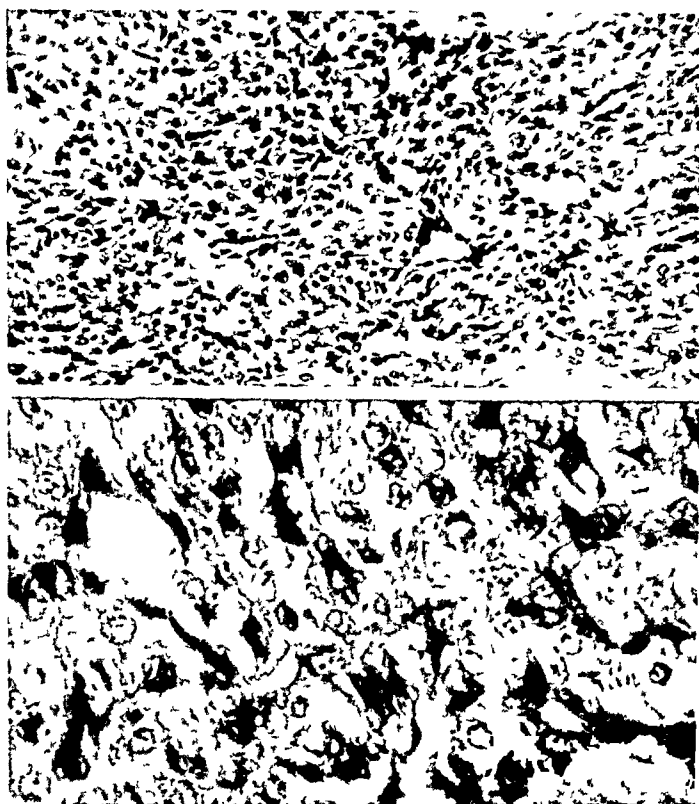


FIG 1—Case 1. Above is shown one of the nodules composed of endothelium-lined capillaries surrounded by masses of pericytes. Below a detail enlargement from another area showing endothelial sprouts both with and without lumens. The endothelia are deeply stained and are in sharp contrast with the rounded pericytes which are paler and have vacuolated cytoplasm.

The second group includes cases with both rounded and spindle-shaped cells

Case 5—At birth, this male infant had a painless nodule, 17×10 Mm, in the right anterior chest wall which did not increase in size. It lay within the pectoralis major muscle and was excised at the age of two months. The case was not followed. The specimen showed a central area of necrosis surrounded by a grayish-white zone of viable tissue, which invaded the muscle to a limited extent (Case made available by Dr Beryl Paige, Babies Hospital, N. Y.)

Case 6—Male. At age 21, his right infra-orbital region was hit with a nail. In a few days a tumor appeared and grew slowly. Three years later it was excised but promptly recurred, and at age 25, it was again incompletely excised. It then grew slowly for 17 years, and more rapidly during the succeeding three years. At age 45, 24 years after onset, it was 4 cm in diameter. It was soft, not tender and had never been painful. It lay 1 cm beneath the epidermis, was apparently encapsulated, and extended into the orbit. The cut surface was pale pink, soft, homogeneous, and mottled with hemorrhages. The case was not followed.

Case 7—Male, age 31. There was a nodule covered with epidermis, pedunculated, and 5 Mm in diameter, which projected from the auricle and had been present since childhood. There had been recent slight increase in size but no pain. It was excised and the case was not followed.

Pathologic Characteristics—In Case 5 the tumor is made up of lobules composed chiefly of endothelial-lined tubes often containing erythrocytes. Arranged in close proximity to the endothelia are rounded pericytes in many areas. In some, however, the cells are spindle-shaped and suggest the appearance of smooth muscle but usually lack myofibrils. In several areas, however, it is possible to trace a direct continuity between these elongated cells without myofibrils and characteristic, mature smooth muscle cells with definite myofibrils. Transition forms containing immature myofibrils can be identified (Fig 2). Case 6 is like Case 5, but no myofibrils can be found and there are no transitions from spindle cells to smooth muscle cells. Case 7 has very few rounded pericytes and is composed largely of spindle-shaped cells which are heaped up in considerable numbers so that the endothelial-lined tubes are often quite widely separated.

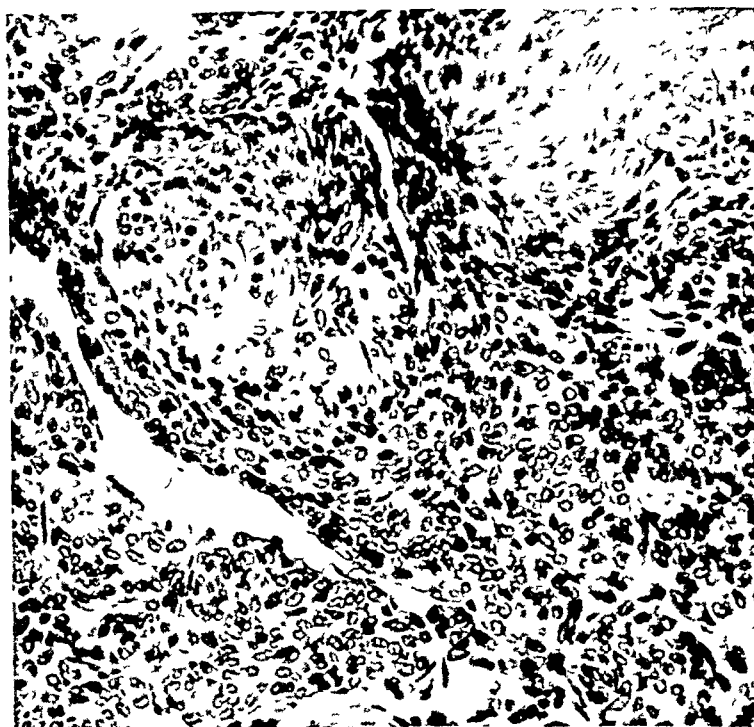


FIG 2—Case 5. Numerous endothelial-lined capillaries are surrounded by rounded pericytes. In places these blend with elongated cells which approximate the appearance of smooth muscle cells.

These three cases seem to us to be of importance because they suggest very strongly that the pericyte is a modified smooth muscle cell. The next step in differentiation would be to have no rounded pericytes but only spindle-shaped cells, some of which were without myofibrils, while the majority were fully differentiated smooth muscle cells. Such tumors exist and have been reported by one of us (A. P. S.) in a paper on cutaneous leiomyomata. They were there called vascular leiomyomata, and the fact that some of the cells contained no smooth muscle fibers was not brought out because its importance was not appreciated. The large amount of smooth muscle formed in the spaces between the vessels was the reason for calling these tumors leiomyomata, but there is no doubt that they are related closely to this present group of hemangiopericytomata.

The next case shows that tumors of this class can exhibit aggressive, infiltrative growth bordering on malignancy

Case 8—Male At age 42, a small tumor appeared on the lateral aspect of the left index finger. This ruptured spontaneously, with a bloody discharge. During the next 11 years he had ten local operations in attempting to remove all of the tumor, but none succeeded. It always reappeared, extending slowly toward the base of the finger and forming multiple nodules. At age 53, the finger was disarticulated at the metacarpophalangeal joint. The tumor reappeared in the stump, and a year later the cicatrix together with the distal three-fourths of the index finger metacarpal bone was resected. This was successful in removing all of the tumor. He was seen 14 years later, without evidence of neoplasm and finally died of an unreported cause at age 70, 28 years after the tumor first appeared, and 16 years after the last operation.

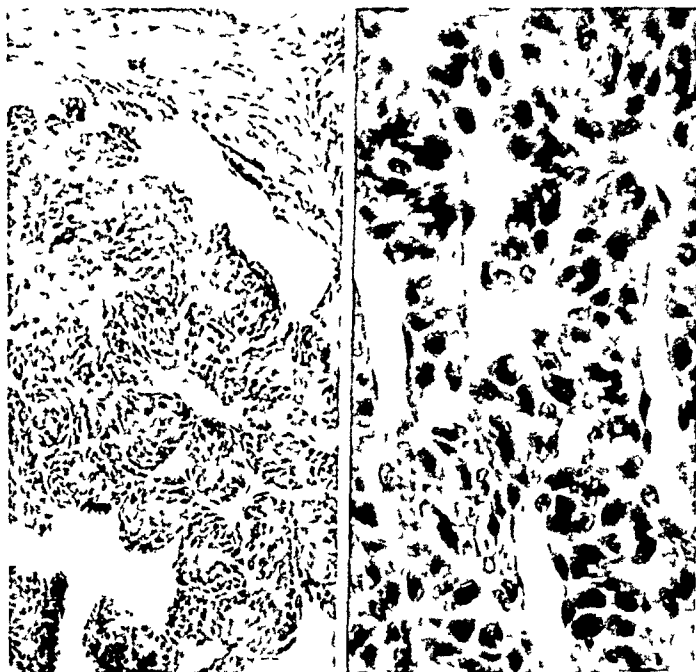


FIG. 3—Case 8. Appearance of the tumor in the stump of the amputated finger. At the left, a nodule of tumor with its endothelial tubes surrounded by pericytes. At the right, a detail in higher magnification.

In this tumor the pericytes are always the most conspicuous feature of the growth (Fig. 3). Capillaries and endothelial sprouts are present but as the sprouts are not canalized they are inconspicuous and can easily be overlooked. Nevertheless, they are always formed and the tumor grows characteristically in lobules made up of aggregations of vessels and sprouts with their satellite cells. Grossly, the tumor nodules were soft and pallid, presumably because they contained so little blood. Unfortunately, the tissue obtained from this tumor was never properly fixed and our cytologic studies leave much to be desired.

The last case is an example of late metastasis and death in a hemangio-pericytoma that exhibited a number of interesting variations in the primary growth.

Case 9—Colored female At age 34, she first noted a swelling on the medial aspect of the lower part of the right thigh. This grew considerably during the next three years until, finally, it became slightly painful on walking and its bulk caused slight limitation

of motion at the knee joint. It was excised at age 37. The tumor was irregularly ovoid and measured 14x7x6 cm. It was intimately attached to the periosteum of the anterior aspect of the femur between the condyles and to the mesial aspect of the capsule of the knee joint. Throughout the rest of its extent, it was enclosed by a capsule. The tumor

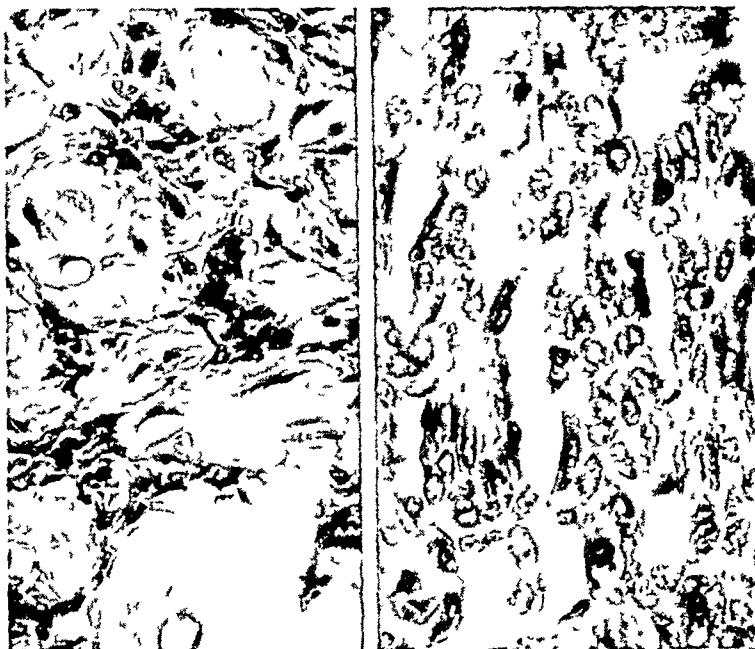


FIG 4—Case 9. Detail from the primary tumor. At the right, endothelial tubes and pericytes, without much fibrosis. At the left, the capillaries are surrounded by dense thick collagen sheaths and the pericytes pushed aside and atrophic.

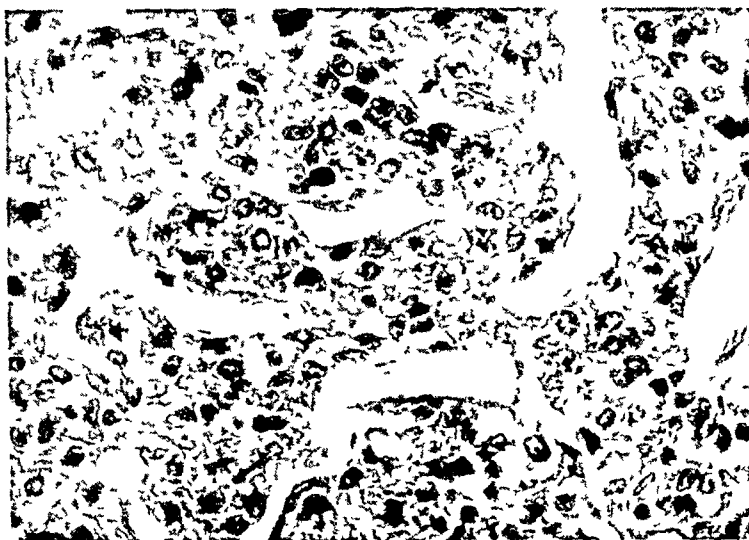


FIG 5—Case 9. Metastasis in the liver. The tumor maintains the relationship of capillary tube and surrounding pericytes but the fibrous elements are much less.

was composed of many pale and reddish nodular masses. There was never any local reappearance but four years later there were found five nodules in the right lobe of the liver, varying from 1 to 4 cm in diameter and one of them was biopsied. The iliac and celiac nodes were enlarged. The liver was treated postoperatively with small doses of roentgenotherapy, with relief of pain. Seventy-four months after the first operation there was roentgenographic evidence of metastases in the third and fifth ribs, and these also received roentgenotherapy. She went progressively downhill, and finally died seven years and four months after the first operation and three years and four months after proof of liver metastases. No autopsy was done.

Pathologic Characteristics—Histologically, the primary tumor is composed of capillary tubes and sprouts which in some areas are surrounded by layers of rounded and occasionally elongated cells in the customary fashion. Where recent growth has occurred, the capillaries are simple endothelial tubes supported by reticulin fibers, but where the tumor is older, the endothelia are surrounded by thick compacted collagen sheaths of a hyaline aspect in ordinary stains and the tumor cells are outside of these (Fig 4). The growth of pericytes, occasionally, is so massive that the vessels are widely separated but, as a rule, the vascular nature of the tumor is never in doubt. No myofibrils are recognized in any of the tumor cells. Laidlaw stains show a rich reticulin framework which surrounds most of the tumor cells.

The vascular aspect of the tumor is clearly shown in the liver metastasis, which is composed of many endothelial tubes surrounded by rounded cells so closely placed that the tumor cells of one unit often touch those of its neighbors (Fig 5). Most of the tumor cells are surrounded by delicate collagen or reticulin fibers. The aspect of this metastasis closely resembles parts of the original tumor and, histologically, does not appear like a malignant growth.

The hemangiopericytoma thus emerges as a tumor which does not have sufficiently arresting gross features to enable one to recognize it clinically. Except in Cases 2 and 3 in which the tumors involved the skin and resembled other congenital hemangiomata, there is no red color nor are there other gross characteristics suggesting that the growth is one of blood vessels. This is due apparently to the accumulation of pericytes and connective tissue in which the vascular tubes are incased and also to the fact that many of the endothelial sprouts are not canalized and contain no erythrocytes. Otherwise, it behaves very much like other angiomatous tumors in its tendency to begin before birth or early in life, to grow locally sometimes as a circumscribed nodule, sometimes with slow and limited infiltration of surrounding tissues, occasionally with more persistent and aggressive infiltration and rarely with metastasis. Although usually small, it may attain a very considerable size, up to a length of 14 cm as is shown by Case 9.

The diagnosis can be made by histologic examination. The tumor must be composed of groups of endothelial-lined tubes or impervious endothelial sprouts surrounded by rounded cells with a supporting meshwork of reticulin fibers. The rounded cells may show a tendency to become elongated and in this form poorly defined myofibrils may be found. Usually, the vessels with their pericytes are distinct one from the other, separated by a fibrous stroma, but they may become so closely packed that the pericytes of one vessel may be in continuity with those of its neighbors. One should be very certain, however, that the growth is basically vascular and not a tumor whose cells are nourished by a rich vascular network such as one sees in many tumors of endocrine organs, in some Ewing tumors of bone marrow, and elsewhere.

SUMMARY

A type of vascular tumor has been described, characterized by the formation of endothelial tubes and sprouts with a surrounding sheath of rounded and sometimes elongated cells. The writers believe that these are derived from the capillary pericytes, described by Zimmermann, and suggest that the tumors be called hemangiopericytomata.

BIBLIOGRAPHY

- Murray, M R, and Stout, A P The Glomus Tumor Investigation of Its Distribution and Behavior, and the Identity of Its "Epithelioid" Cell Am Jour Path, 18, 183, March, 1942
- Orsos, F Gefasssprossgeschwulst (Gemmangioma) Beitr z path Anat, 93, 121, 1934
- Schmidt, H Zur Kenntnis des Gemangioms und seiner Beziehungen zum Angiosarkom Frankfurt Ztsch f Path, 51, 43, 1937
- Stout, A P Solitary Cutaneous and Subcutaneous Leiomyoma Am Jour Cancer, 29, 435, 1937
- Zimmermann, K W Der feinere Bau der Blutcapillaren Ztsch f Anat u Entwicklungsgesch, 68, 29, 1923

THE PATHOGENESIS OF MIXED TUMORS OF THE SALIVARY GLAND TYPE

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THE CONTROVERSY concerning the fundamental structure of mixed tumors of the salivary gland type has never been settled satisfactorily. Since 1853, when the tumors were recognized as a clinical entity by Paget,¹ the ensuing years have added much discussion as to their nature. In 1859, Theodor Billroth² wrote his classic thesis on salivary gland tumors and surprisingly little of morphologic interest has been added since his excellent description. His interpretation of the tumors as mesenchymal growths (accepted with certain modifications by Virchow) held sway for many years, overshadowing the earlier work of Robin,³ and others, who suggested that the tumors were epithelial. Toward the latter part of the nineteenth century, Billroth's concept of the tumors was challenged, and since then numerous other theories of histogenesis have been presented. One of the best and most inclusive summaries of these theories is that of Hoepfel,⁴ to which the reader is referred. Hoepfel divides the theories of the nature of mixed tumors into three main groups, based on the interpretation of the parenchymal elements of the tumors.

(1) In this class fall all of those conceptions holding that the parenchyma is mesenchymal in origin. Billroth originated this idea. Virchow⁵ felt that the epithelium was derived from mesenchyme, due to the ability of the connective tissue elements to undergo metaplasia into epithelial tissues. Others believed that the tumors were composed of endothelial cells, and for many years the tumors were called "endotheliomas."

(2) In this large group fall those theories considering the parenchyma as derived from epithelium. However, while there is agreement concerning the origin of the parenchyma, there are differences in interpretation of the nature of the stroma. These latter opinions may be divided into five subgroups, which regard the stroma in the following ways: (a) The stroma takes origin by displacement of mesodermal germ tissue at the same time in embryonic life as do the ectodermal elements. (b) The stroma is mesodermal tissue which is formed as the result of the improper local "organizer" action of the epithelium on undifferentiated mesoderm. This utilizes the present-day knowledge of experimental embryology. (c) The stroma is a mesodermal tissue which has been formed by metaplasia of the epithelial parenchyma. (d) The stroma is epithelium which has been modified as a result of its secretory products so that it resembles cartilage and other mesodermal tissues. (e) The stroma is a

"hybrid" substance arising through the union of epithelial and mesothelial tissues with their secretory products

(3) In this small group are included those persistent ideas that the parenchyma possesses epithelial as well as endothelial components. Evidence in support of such a conception has been so vague that little acceptance is given this idea at the present time.

In the American and English literature perhaps the most generally accepted theory held at present is that mixed tumors are true epithelial tumors without mesodermal elements. There are several standard textbooks of pathology that subscribe to this conception. However, during the past decade there has been a trend, particularly in the German literature, to regard the tumors as primary epithelial growths which have induced abnormal differentiation of the undifferentiated mesoderm.

When one examines the evidence for all of these theories mentioned above, it is apparent that they are based on individual interpretations of the morphology of the pleomorphic tumors. One needs only to examine sections of mixed tumors to realize how unsatisfactory and difficult morphologic study may be. All variations within a tissue and gradations between tissues are found. To illustrate the difficulties involved in histologic study of the tumors, let us consider their microscopic appearance very briefly.

HISTOLOGIC FEATURES OF THE MIXED TUMORS

The parenchyma of the tumors is unquestionably epithelial and appears in many variations. The small oval or spindle cells growing in sheet formation represent one of the most common types. They closely resemble the type of cell seen in basal cell carcinomata. Occasionally the cells are larger, with vesicular nuclei. They often form acini, which may contain mucus. Some of the individual cells show evidence of secretion in the form of intracellular droplets of mucus. Epithelial cells with intercellular spinous processes in bulbous formation with typical epithelial pearls are often found. Some of the epithelial cells form pseudorosettes, resembling embryonic ducts more closely than they do adult epithelial structures. Occasionally nests of epithelium show a peculiar type of degeneration of their central portions with the resultant formation of star-shaped cells similar to those seen in ameloblastomata. These cells may be widely separated but usually remain connected by long intercellular processes.

The epithelial cells are separated by a stroma, the appearance of which suggests mesodermal origin. The most characteristic form of the stroma is the chondromyxomatous tissue. The myxomatous tissue bears a striking resemblance to the connective tissue found in the umbilical cord, and that occasionally seen in chondrosarcomata. It is composed of branching cells embedded in a matrix of homogeneous mucoid substance. The cell bodies are usually triangular in shape with long, branching pseudopodia. The amount of cytoplasm enclosing the deeply-staining nuclei is small but the branching processes, of which there are usually two or three, extend far out into the

intercellular substance. Often there are additional more delicate fibrillary processes arising from other parts of the cell bodies. These cells may be widely separated or may form strands of two or three. The cartilaginous or "pseudocartilaginous" tissue differs from adult cartilage only in the absence of the characteristic pattern. Other tissues found in the stroma resemble hyalinized connective tissue, with eosinophilic, dense homogeneous matrix containing a few elongated cell bodies. Adult fat cells and small islands of bone are occasionally found deep within the tumor nodules.

The types of tissue mentioned above are well recognized. Their relationship, however, is interesting and peculiar to this type of tumor. Epithelial tissue of one type appears to change gradually into another type. Myxomatous tissue merges into cartilaginous tissue or into hyalinized connective tissue. Even more puzzling than this, however, is the anatomic relationship between the epithelium and the stroma. Where the epithelium is well differentiated there is a sharp line of demarcation, but in many places there is gradual, apparent transformation of frank epithelium into myxomatous tissue. In these transitional zones the cells cannot be said to be either epithelial or myxomatous.

It is this unusual relationship of tissues which appear to be derived from separate germ layers that is responsible for the confusion regarding the histogenesis and nature of these tumors. It seems incredible that epithelial cells can resemble mesenchymal tissues so closely. Yet if there are two types of tissue how can one explain their intimate relationship and apparent transitions from one into another? A morphologic study of the tissues has failed to provide a satisfactory answer to this question.

HISTOCHEMICAL INVESTIGATION OF MUCOID TISSUES OF MIXED TUMORS

In considering a group of mixed tumors of the salivary gland type, the futility of further study of their morphology at once became evident. It occurred to us that a chemical investigation of the mucoid material in the parenchyma and stroma might be of value in determining the nature of the tissues and, accordingly, a microchemical study of epithelial and mesodermal mucoids was undertaken by one of us (L. H. H⁶). Before describing the results of this study it will be of value to discuss briefly the chemistry of the mucopolysaccharides. For a more detailed discussion the reader is referred to the classic monograph of Levene,⁷ as well as the more recent articles of Meyer.⁸

Mucoproteins are complex proteins composed of two radicals, one a protein molecule, the other a carbohydrate complex. It is the latter group which is responsible for the specificity of the molecule and hence its chemical and staining properties. According to Levene the prosthetic groups are composed of a hexosamine fraction conjugated with sulfuric, glucuronic and acetic acids. They exist as several modifications of one general type, the best known ones being chondroitin sulfuric acid and mucosin sulfuric acid. These compounds are similar in structure and composition, differing only in the carbohydrate

fractions (which are probably isomeric hexoses) as well as in the attachment of certain side-chains

Despite the chemical similarity of these mucoproteins, their distribution in nature is widely different. Chondroitin sulfuric acid has been isolated only from mesenchymal tissues such as cartilage, bone, tendon, sclerae, umbilical cord, and the wall of the aorta. The chondroitin sulfuric acid protein complex, therefore, has been said to be the mucoprotein of connective tissue,⁴ and is probably responsible for the staining characteristic of the mesenchymal mucoids. Mucoitin sulfuric acid on the other hand has been found in the mucin of salivary glands and gastric mucosa, in serum mucoids, ovomucoid, Wharton's jelly, vitreous humor, and in the cornea. Recently, however, evidence has been presented that the mucoids of Wharton's jelly, and egg white do not contain mucoitin sulfuric acid. The subject of mucopolysaccharides has been further complicated by the identification of sulfate-free mucopolysaccharides in Wharton's jelly and salivary gland mucin.⁵ It might be said, however, that the mucoitin sulfuric acid complex is a product of epithelial secretion, while chondroitin sulfuric acid protein is limited to those connective tissues of mesenchymal origin.

Because of the chemical similarity of their prosthetic groups, the tissue mucoids stain alike with basic and metachromatic dyes. For this reason it has not been possible to distinguish between them by ordinary staining procedures. Recently, one of us (L. H. H⁶) has devised certain microchemical methods by which mesenchymal and epithelial mucoids (presumably chondroitin sulfuric acid and mucoitin sulfuric acid complexes, though the simpler mucopolysaccharides known to exist in epithelial mucus, may play some rôle in the chemical reaction) can be differentiated in fixed tissue sections. One of these is a titration method utilizing the difference in affinity of the protein complexes for very dilute aqueous solutions of the metachromatic dyes. Serial sections of formalin-fixed tissue are stained with increasing dilutions of toluidine blue or polychrome methylene blue. There is a definite range of dilutions (in the case of polychrome methylene blue about 1:200 to 1:1400 depending on the temperature, the age, and the method of preparation of the stock solutions) in which the chondroitin sulfuric acid complexes stain with almost maximum intensity while the epithelial mucoids fail to stain. In the control experiments it has been possible to stain cartilage, chondrosarcomatous tissue and the mucoid degenerative products in the walls of arteries with dyes of the proper dilution while the epithelial glands and secretions of the respiratory, gastro-intestinal and biliary tracts and salivary glands failed to stain unless stronger solutions were used. This is a delicate method and requires considerable experimentation with control tissues to obtain the proper dilution for good differentiation.

Another method of differentiating the mucoids is based on the greater resistance of the mesenchymal mucoids to hot acid. Incubating paraffin cut-sections of tissue with dilute solutions of sulfuric acid changes the tissue mucoids in such a way that they no longer stain with the metachromatic dyes.

This, presumably, is due to the breakdown of the acid complex, as the characteristic color is said to be dependent upon the sulfuric acid ester linkage. The rate of breakdown is different for the mesenchymal and epithelial mucoids. Care must be taken that large enough quantities of acid be used to rule out differences due to disproportionate concentration of mucoid substance.

FIG 1



FIG 2



FIG 3



FIG 4

FIG 1—Mixed tumor of the parotid gland stained with polychrome methylene blue 1:340. The matrix of the cartilaginous tissue stains bright reddish purple (photomicrograph was taken with a green filter to emphasize this color) while the remaining tissue stains blue or green. Epithelial mucus, as represented by gastrointestinal, biliary, and salivary glands, failed to stain with this dilution.

FIG 2—Mixed tumor of the parotid stained with differential polychrome methylene blue solution described in Figure 1. The wavy strands in the upper right portion of the photomicrograph represent reddish purple mucus of a myxomatous area. Intracellular mucus failed to stain with this dilution.

FIG 3—Mixed tumor of salivary gland stained with 1:260 aqueous dilution of polychrome methylene blue. Note the intracellular mucus which failed to stain with the differential solution used in Figures 1 and 2. The intracellular mucus in goblet cells of adjacent salivary gland behaved as the above type of mucus.

FIG 4—Mixed tumor of the parotid gland stained with 1:260 polychrome methylene blue. The mucus within the tumor also failed to stain with the differential solution used in Figures 1 and 2. This type of mucus as well as that in Figure 3 was destroyed by hot sulfuric acid in the same manner as the initial types of epithelial mucus.

While the end-points of this method are not as sharp as they are in the first, the results are consistent, and can be used in the evaluation of the chemical nature of the mucoids.

Both methods show that the mucoid in the myxomatous and cartilaginous areas in mixed tumors of the salivary glands behaves exactly as does the chondroitin sulfuric acid complex in skeletal cartilage, chondromata, chondrosarcomata, and in the walls of arteries showing mucoid degeneration (Figs

1 and 2) The mucoid within the acini stains exactly as does the mucoprotein complex in the mucin of the salivary gland, gastro-intestinal and respiratory tracts, as well as that in mucoid carcinomata of the intestine (Figs 3 and 4)

From the results of these experiments, it seems justifiable to conclude that the mucoid substance in the myxomatous and cartilaginous areas is a chondroitin sulfuric acid complex while that secreted by the epithelial cells of the tumors is a different mucoprotein, probably mucitin sulfuric acid complex as well as perhaps simpler mucopolysaccharides

Since the mucoid in the cartilaginous and myxomatous areas is a mesodermal mucoprotein, presumably chondroitin sulfuric acid, and since the tissue presents the morphologic appearance of mesodermal structures, it is probable that these tissues are truly mesodermal. It does not seem likely, as Techouyeres¹⁰ suggests, that there is a reciprocal mutation between the chemical forms of mucitin and chondroitin sulfuric acid. This chemical change, involving a special rearrangement of a molecule and perhaps other changes, has never been shown to occur. Similarly, the metaplasia of epithelial cells into true cartilage and myxomatous tissue after histodifferentiation has taken place is contrary to present embryologic concepts. We conclude, therefore, that there are two types of tissue, mesenchymal and epithelial, in mixed tumors of the salivary gland type.

It is not possible to say whether the myxomatous areas represent phases of rapidly growing tissues or whether they are areas of degeneration or the result of local vascular change. They are usually quite avascular, though one occasionally sees blood vessels within such an area. The similarity between such myxomatous tissues and certain types of chondrosarcoma is striking. The similarity is more than just a structural one. When stained with dilute acid solutions of ortho-Capill blue (an oxidation product of methylene blue*) the branching type of cell structure is demonstrated unusually well. The intercellular substance of myxomatous and chondrosarcomatous tissue fails to stain with the Capill blue, whereas that in adult cartilage stains intensely. With transformation from myxomatous to adult tissue there is a gradual appearance of the stainable substance (Figs 5 and 6). The chemistry of the intercellular matrix of cartilage has not been worked out well enough to enable us to understand this completely, but it is quite possible that this stainable substance is chondro-albuminoid. Very little is known of this substance except that it is an albuminoid closely related to osseo-albuminoid, and similar in many respects to elastin and keratin. The ground substance of cartilage, the keratin layer of epithelium, the elastic layer of blood vessels, cell nuclei and cytoplasm, hyalin and collagen fibers, serum and egg albumin, epithelial mucoid and serous secretions are all stained intensely by Capill blue. The intercellular substance of the myxomatous areas in the mixed tumors, which stains intensely with mucoid stains and that in the histolog-

* The dye was prepared by boiling an aqueous solution containing several drops of 1:100 o-Capill blue and several drops of dilute hydrochloric acid per 50-60 cc of water.

ically similar chondrosarcoma, are the only protein substances which have been found not to take the blue stain

FIG 5 A

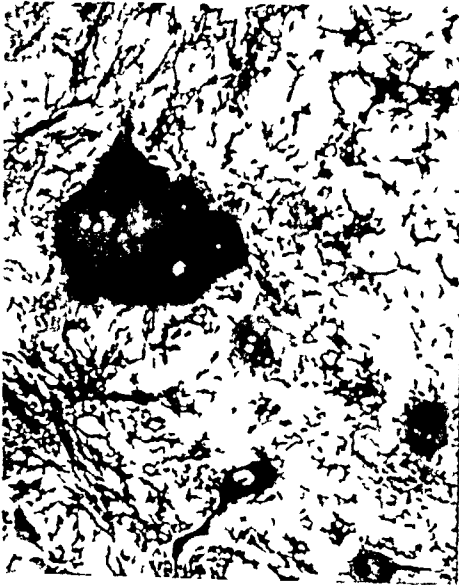


FIG 5 B

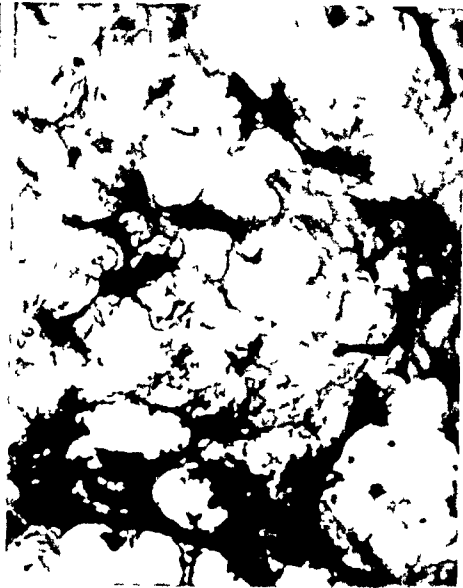


FIG 6 A

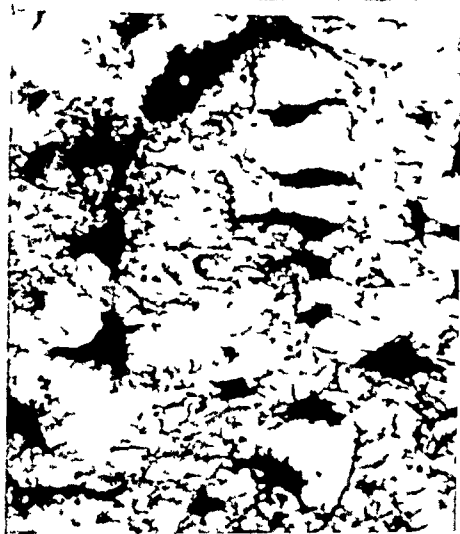


FIG 6 B

FIG 5—(A) Mixed tumor of the submandibular gland stained with orthoCran blue. Note that the intercellular substance of the myxomatous tissue fails to stain while that of the small island of cartilage is deeply colored.

FIG 5—(B) Higher magnification of myxomatous cells showing details of branching structure.

FIG 6—(A) Chondrosarcoma of the chest wall stained with orthoCran blue. Note that the intercellular substance fails to stain as is the case in the myxomatous tissue of Figure 5 A. Note also the similarity of structure between these cells and those in the myxomatous areas of the mixed tumor.

FIG 6—(B) Higher magnification showing similarity to Figure 5 B.

PATHOGENESIS OF THE MIXED TUMORS

If it is accepted that there are two types of tissue in mixed tumors, certain theoretic concepts as to their pathogenesis can be formulated. In view of the presence of two different types of tissue, both of which lack normal differentiation, a failure of normal development seems probable. Evidence continues to

accumulate in support of the fact that normal development depends upon a closely integrated interrelationship between all tissues involved. Functional inadequacy on the part of one tissue at any phase during development may result in structural changes in all tissues concerned subsequently. Such "organizer" or "provocative" action of epithelium on the undifferentiated mesoderm, and *vice versa*, in the formation of certain types of tumors has been suggested before. This view has been proposed by Nottenbrock,¹¹ after Schuimann and Pflüger's work on the histogenesis of craniopharyngiomas. Such an explanation has been used for mixed tumors of other regions of the body. Schmidt¹² has applied this principle to mixed tumors of the breast, and Mollet,¹³ and, more recently, Womack and Graham,¹⁴ have used it to explain certain tumors of the lung.

In line with embryologic evidence, the buccal ectoderm of the salivary gland *anlage* probably affects the surrounding buccal mesoderm. In turn, differentiation and development of the ectoderm is probably influenced by the buccal mesoderm. There is considerable evidence that even adult epithelium retains a certain amount of "organizer" influence. Huggins¹⁵ has shown that bladder epithelium is capable of causing differentiation of adult fibrous tissue into bone. This indicates that there are undifferentiated cells in adult fibrous tissue capable of formation of more highly specialized structures. That fibrous tissue is capable of influencing the growth and differentiation of epithelium is shown by the experiments of Drew.¹⁶ He has found that tissue cultures of kidney epithelium and cancer cells from breast carcinomas grow in sheet formation unless fibrous tissue cells are present in the culture. In the latter case, the tumor cells differentiate to form duct-like structures. There is nothing specific in the buccal mucosa which possesses the properties of influencing the differentiation of mesoderm in the manner seen in mixed tumors of the salivary gland type, since the epithelium of the lacrimal gland and skin are capable of similar tumor formation.

The experimental disturbance of tissue environment of the embryo has been shown to lead to structural malformations.¹⁷ It is possible that some such disturbances may lead to development of mixed tumors of this type. The time during embryonic life that such a disturbance occurs, as suggested by Li and Yang,¹⁸ would account for the degree of differentiation which the tissues show. Those occurring earlier in life have the greater potentialities of differentiation.

This interrelationship of tissues has been almost completely ignored in the case of mixed tumors of the salivary gland type but has been used to explain the development of teratomata.¹⁹⁻²⁰ This utilization of the "organizer" conception regards the tumors as a result of primary epithelial maldevelopment, with mesodermal differentiation secondary to this epithelial disturbance. Though the application of this theory to mixed tumors of the salivary glands is not subject to experimental proof at present it seems to us to be the most rational and is thoroughly in keeping with present-day embryologic tenets.

CONCLUSIONS

(1) The theories of the pathogenesis of mixed tumors of the parotid gland are briefly summarized

(2) A method is described by which, with special staining technics, mesenchymal mucus can be differentiated from epithelial mucus. Both of these substances are found to be present in mixed tumors of the parotid gland

(3) In view of the fact that epithelial and mesenchymal mucoids are believed to be identified, it is suggested that two tissue components are represented in these tumors, and that the tumors are, therefore truly mixed tumors

(4) It is suggested that the origin of these tumors might be best explained on the basis of embryonic alteration in tissue relationships, in accordance with the "organizer" theory of Spemann

REFERENCES

- ¹ Paget, Jr. Lectures on Tumors. London, Longmans, 1853
- ² Billroth, T. Beobachtungen über Geschwülste der Speicheldrüsen. Virchows Arch, 17, 357, 1859
- ³ Robin and Laboulbène. Memoire sur Trois Productions Morbides non decrites. Compt rend Soc de Biol, 5, 185, 1853
- ⁴ Hoepfel, W. Bau und Wesen der Schleimdrüsen- und Mischgeschwülste am Gaumen und im Mundhohlenbereich insbesondere in ihren Beziehungen zu den sog. Speicheldrüsenmischgeschwülsten. Ztschr f Hals-, Nasen-, und Ohrenheilkunde, 41, 52, 1936-1937
- ⁵ Virchow, R. Vorlesungen über Pathologie. Bd II. Berlin, Hirschwald, 1863
- ⁶ Hempelmann, Jr., L. H. Staining Reactions of the Mucoproteins. Anat Rec, 78, 197, 1940
- ⁷ Levene, P. A. Hexosamines and Mucoproteins. London, Longmans, 1925
- ⁸ Meyer, K. The Chemistry and Biology of Mucopolysaccharides and Glycoproteins. Cold Springs Harbor Symposia on Quantitative Biology, 6, 91, 1938
- ⁹ Blau, G., Oldfeldt, C., and Karlberg, O. Zur Chemie der Mucine und Mucoide. Ztschr Physiol Chem, 3, 234, 1935
- ¹⁰ Techouyeres, E. La Genesis du Tissu Cartilagineux dans les Tumeurs Mixtes des Glandes Salivaires. Ann d'anat Pathol, 11, 905, 1934
- ¹¹ Schurmann, Pflüger, and Norrenbrock. Die Histogenese Ekto-Mesodermaler Mischgeschwülste der Mundhöhle. Georg Thieme, Leipzig, 1931
- ¹² Schmidt, I. Zur Frage der Entstehung der Mischgewebe und Hand von zwei Fällen von Milchdrüsenmischgeschwülsten des Hundes. Virchows Arch, 291, 491, 1933
- ¹³ Moller, A. Zur Entstehung der Lungenmischgeschwülste. Virchows Arch, 291, 478, 1933
- ¹⁴ Womack, N., and Graham, E. A. Mixed Tumors of the Lungs. Arch Pathol, 26, 165, 1938
- ¹⁵ Huggins, C. B. The Formation of Bone Under the Influence of Epithelium of the Urinary Tract. Arch Surg, 22, 377, 1931
- ¹⁶ Drew, A. H. Growth and Differentiation in Tissue Cultures. Brit Jour Exper Path, 4, 46, 1923
- ¹⁷ Stockard, Chas. R. Developmental Rate and Structural Expression. Am Jour Anat, 28, 115, 1920-21
- ¹⁸ Li, R. L., and Yang, C. S. An Inquiry into the Origin of Mixed Tumors of the Salivary Glands, with Reference to Their Embryonic Interrelationships. Am Jour Cancer, 25, 259, 1935
- ¹⁹ Nicholson, G. W. The Histogeny of Teratomata. Jour Path and Bacteriol, 32, 365, 1929
- ²⁰ Willis, R. A. Structure of Teratoma. Jour Path and Bacteriol, 40, 1, 1935

ADENOLYMPHOMA OF THE PAROTID GLAND

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ADENOLYMPHOMA is one of the rarer salivary gland tumors. Although several times reported in the pathology literature, it is less well known to clinicians. The purpose of this paper is to discuss the neoplasm from the standpoint of the latter group.

In the last 50 years there have been some 48 cases of the tumor described. In addition to these, however, there are many which have been diagnosed but not reported. Carmichael, Davie, and Stewart² mention several in addition to their own eight examples, and others have been studied by Klempeier,⁷ Stout,¹³ and Weller.¹⁵ The figures to be quoted in this communication are gathered from all the reported instances, plus 16 additional previously unpublished cases. With the increasing interest in Tumor Clinics, other cases will undoubtedly turn up, and occasion the consideration of appropriate therapy. More data are needed concerning the life history of this tumor, the relative proportion of benign to malignant cases, the incidence of recurrences, the effectiveness of surgical excision, the need (if any) for supplementary radiation, and the choice between surgery, radiation, and other therapeutic procedures.

Age Incidence —The great majority of patients were middle-aged or over. Eighty-four per cent of the patients were age 40, or more, with 75 per cent in the fifth, sixth, and seventh decades. At the extreme ends were a child of two and one-half years and a man age 92. The average age was 52 years (Table I).

TABLE I
AGE INCIDENCE

Years	No. of Cases
1- 10	2
11- 20	2
21- 30	1
31- 40	5
41- 50	13
51- 60	20
61- 70	13
71- 80	4
81- 90	0
91-100	1
Youngest—2½ years	
Oldest—92 years	
Average—52 years	

Sex —Of the 62 cases where the sex was stated, 50 were males and 12 females. The male to female ratio is, therefore, almost five to one.

Duration of Symptoms —Adenolymphomata are slow growing tumors.

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The duration of symptoms varies widely, ranging from a few months to 30 years. Table II shows that about 80 per cent of the patients complained of a mass which had been present for from several months to four years.

TABLE II
DURATION OF SYMPTOMS
(where definitely stated)

	No. of Cases
1-6 months	8
6-12 months	13
1-2 years	6
2-3 years	6
3-4 years	4
4-5 years	1
5-10 years	3
10-15 years	1
More than 15 years	2

Clinical Course—In general, it may be said that the tumors are present for at least several months before a physician is consulted. During this time the swelling may vary somewhat in size, but does not change very much. At some time, however, the growth-rate has usually accelerated, probably due to rapid accumulation of fluid in the cystic spaces, and it is then that the patient has become concerned and sought professional advice.

The diameter of the tumor at the time of the first examination varies from one to four or five centimeters, and is usually described as being the size of an almond, a cherry, or even a small orange.

In consistency, the tumors are usually firm and solid. Rarely they are hard, sometimes grossly cystic and fluctuant. The growths are ordinarily attached to the deeper structures, but not adherent to the skin. Consequently, the latter can be moved over the underlying tumor, but the mass itself cannot be shifted.

Except when secondarily infected, there is no tenderness on palpation, nor are the tumors usually painful. Occasionally, when the mass is undergoing a comparatively rapid growth, there may be some local discomfort. This, however, is inconsiderable, and confined to the tumor site.

Usually the mass has been described as over the angle of the jaw, in the region of the parotid gland. Occasionally, it lies along the ramus of the mandible, and in a few instances is retro-auricular. One case, an exception, is described as being in the neighborhood of a submaxillary gland.¹⁶ Another, reported by Freshman and Kuiland,³ was in the neck, along "the anterior edge of the superior portion of the left sternocleidomastoid muscle."

The number of cases is about evenly divided between the left and right parotid regions.

With two exceptions the tumors have all been unilateral. The first instance of bilateral involvement was reported by F. L. Niño,¹⁰ in 1940. This author has recently reported six cases of adenolymphomata seen in the last 11 years. This represents 10 per cent of the total number of parotid tumors observed at the Clinico-Surgical Institute of the University of Buenos Aires.

The first of the author's cases is bilateral. The second known instance of bilateral involvement occurred in a patient of Dr. A. W. Oughterson's, at the New Haven Hospital, treated in July, 1941, and previously unreported.

Histology—Though it is not within the scope of this report to deal at length with the pathology of adenolymphoma, a brief word may be said about the gross and microscopic appearance of the tumor.

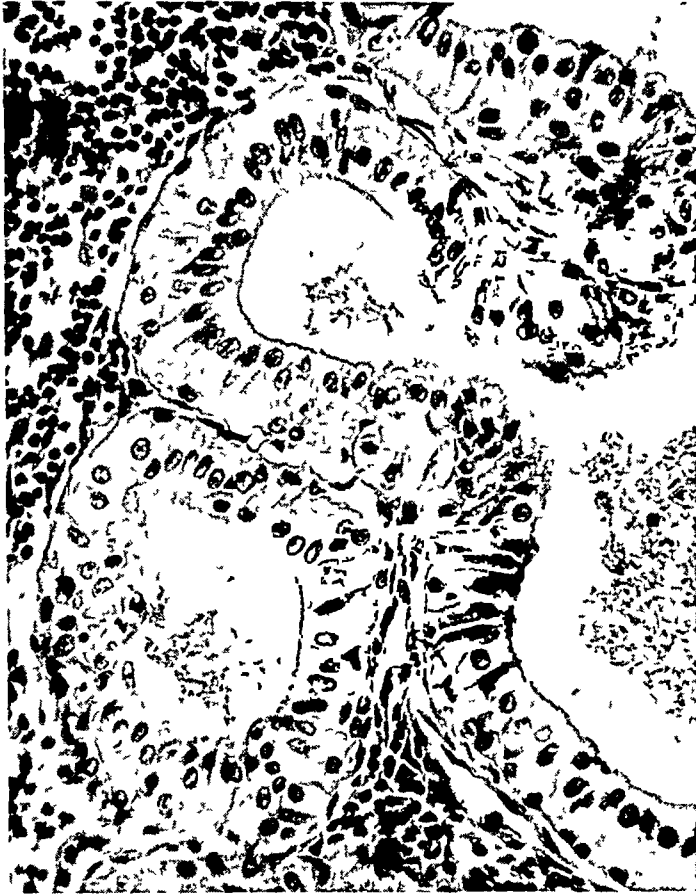


FIG. 1—Adenolymphoma. Cyst wall. (High power)

The neoplasms vary in shape but are usually spherical or ovoid. They have a lobulated, smooth surface, which is usually covered by a thin, adherent capsule. In almost all instances this completely surrounds the mass and separates it from the parotid. Exceptionally, the capsule is incomplete and then the tumor infiltrates the parenchyma of the gland. The substance cuts with ease, revealing a gray-pink cut surface, which is often finely granular and pitted with tiny cystic spaces. The latter vary in diameter from the size of a pinhead to several millimeters or more. From some of the cysts a serous fluid may be expressed.

Microscopically, the stroma is made up of lymphoid tissue with large germinal centers. In the midst of this are numerous and various-sized cysts. Many of these contain papillary projections. The cysts are lined with a double layer of epithelium (Fig. 1). The inner of these layers is usually made up of tall, cylindrical cells. These have a finely granular cytoplasm which

stains pale pink with hematoxylin and eosin. The nuclei are apical, basophilic, and vesicular. Waithin¹¹ described cilia, but they have not been found by others. Between the bases of the tall cells, and less numerous, are small cuboidal cells. These, too, have a pale, granular, acidophilic cytoplasm. Their nuclei are centrally located and vesicular. Many of the cysts contain an amorphous pink material and cellular debris. Others are devoid of secretion. There are few or no mitotic figures. All-in-all, the appearance is that of a benign neoplasm. There are, however, two cases which are reported as showing definitely malignant areas^{11, 12}.

As pointed out by Carmichael, Davie and Stewart,² there are variations in the microscopic appearance of the tumor. This is in agreement with Klemperer's⁷ view that the term adenolymphoma suggests a group of closely related neoplasms rather than a fixed histologic pattern. The three cases reported herewith fit in with the group of variations, yet quite definitely belong to the category of adenolymphomata.

Therapeutic Procedures —

- (1) *Excision Alone* Of the 40 case reports which included the nature of the therapy employed, 38 consisted of excision alone. In two cases where the tumors were completely removed by excision, keloids developed in the scars. These were treated with a radon bulb or roentgenotherapy after the excision.
- (2) *Excision Followed by a Recurrence and Then Secondary Excision* There was one instance of this. The patient, under the care of Dr. C. V. Young, of Bradford, England, had a recurrence of the original tumor three years after local excision. The recurrent tumor was excised ten years after the original operation. According to a communication from Dr. M. J. Stewart, of Leeds, the histology of the original and recurrent tumors was the same, except for some areas of squamous metaplasia in the recurrent tumor.
- (3) *Excision Followed by Roentgenotherapy* There was one patient so treated. He was a male, age 64, who had an adenolymphoma partially excised in the Philippine Islands, May 23, 1939. One week later, because all the tumor had not been removed, he was given ten roentgen ray exposures totaling 1,250 r. During the subsequent month, the tumor continued to enlarge. He was given two more roentgen ray treatments, and then referred to the Memorial Hospital, New York. The diagnosis was confirmed from a submitted slide. No further therapy was administered because the patient developed rectal bleeding, and he returned to the Philippine Islands. A letter received from his physician, one year later, stated that the "remaining tumor is hardly palpable."
- (4) *Irradiation Alone* No cases were treated this way.

Complications—There has been only one reported case of a recurrent tumor. As mentioned above, this was removed by a secondary excision. Histologically, only two instances of definite malignant changes have been reported. This comprises about 3.3 per cent of all known examples of adenolymphoma, the vast majority of which are undoubtedly benign.

One additional case deserves mention. A male, age 54 (Memorial Hospital, Case No. 57792—1939), had an excision of a papillary adenolymphoma in the region of the right parotid gland in 1939. Two weeks before operation a node had been felt beneath the right sternocleidomastoid muscle. About one week following the excision, he developed many enlarged nodes in the right side of his neck. One of these was biopsied and diagnosed as reticulum cell lymphosarcoma. He then developed palpable bilateral axillary nodes. Thereupon, he received deep roentgenotherapy (250 K V) to both sides of the neck and both axillae. In April, 1941 (one year and eight months after the original excision), he had had no recurrence of the parotid tumor, but still had axillary nodes, and was being followed for the reticulum cell lymphosarcoma.

Follow-Up—Due to the difficulties in communication incident to the present war, information is available on the postoperative course of only 26 patients. Of these, two are too recent to be of significance. The remaining 24 may be analyzed as follows:

TABLE III
ANALYSIS OF 26 CASES SHOWING THE TIME-INTERVAL WITHOUT RECURRENCE

Time-Interval	No. of Cases
3 months or less	2
3 to 6 months	2
6 months to 1 year	4
1 to 1½ years	2
1½ to 2 years	3
2 to 3 years	2
3 to 4 years	2
4 to 5 years	2
5 to 6 years	2
6 to 7 years	1
9 to 10 years	1
More than 10 years	1
Total	24

TABLE IV
ANALYSIS OF 64 CASES OF ADENOLYMPHOMA OF THE PAROTID GLAND
48 CASES PREVIOUSLY REPORTED

No.	Source	Patient	Age	Sex	Duration of Symptoms	Treatment	Follow-Up
1	Jaffé R. H. Am. Jour. Cancer 16, 1415 1932		73	M	3 yrs	Excision	
2	Freshman and Kurland Am. Jour. Clin. Path. 8, 422 1938		63	M	1 yr	Excision	Well. No recurrence after 3 yrs.
3	Warthin A. S. Jour. Cancer Res. 13, 116 1929	J. McD. 1931-L-AD	45	M	Many yrs slowly growing	Excision	No information available

TABLE IV—(Continued)

No	Source	Patient	Age	Sex	Duration of Symptoms	Treatment	Follow Up
1	Warthin A S Jour Cancer Res 13, 116 1929	C 1887-L AF	60	M	20-30 yrs recent increase in size	Excision	No information available
5	Stout and Kraissl Arch Surg 26, 485 1933	R M	61	M	2 yrs	Excision	No recurrence after 1 yr
6	Stout and Kraissl Arch Surg 26, 485 1933	D L	71	F	1 yrs	Excision	No recurrence after 3 yrs 2 mos
7	Hildebrandt Arch f klin Chir 49, 167 1898		41	M			Not available
8	Sultan Deutsch Ztschr f Chir 48, 143 1898		44	M			Not available
9	Morestin Bull Soc anat de Paris 4, 709 1902		23	F			Not available
10	Lecene Rev de chir 37, 1 1908		40	F			Not available
11	Lecene Rev de chir 37, 1 1908		50	M			Not available
12	Albrecht and Artz Frankfurt Ztschr f Path 4, 47 1910		61	M		Excision	Author died 1923 Records not available
13	Albrecht and Artz Frankfurt Ztschr f Path 4, 47 1910		12	F		Excision	Author died 1923 Records not available
14	Glass Frankfurt Ztschr f Path 9, 335 1912		65	M	1 yr		Not available
15	Delangade Peyron and Rousieroux Bull de l Assn franc p l'étude du Cancer 7, 370 1914		33	F			Not available
16	Menetrier Peyron and Surmont Bull de l Assn franc p l'étude du Cancer 12, 205 1923		50	M	10 yrs		Not available
17	Mazza and Cassinelli Compt rend Soc Biol 88, 400 1923		36	M	10 yrs		
18	Rükl Zentralbl f allg Path u path Anat 35, 5310 1924		47	M	2 yrs		
19	Askanazy Quoted by Sternberg in Henke Lubarsch Bd 1 Teil 1 333		54	M			
20	Houdard and Hufnagel Bull de l Assn franc p l'étude du Cancer 16, 377 1927		65	M			
21	Spitznagel Wien klin Wchnschr 42, 983 1925		65	M			
22	Spitznagel Wien klin Wchnschr 42, 983 1925		45	M			
23	Carmichael Davie and Stewart Jour Path and Bacteriol 40, 601 1935		63	M	4 yrs	Excision Recur- rence Reexcision	Recurrence 3 yrs after first excision Secondary excision 10 yrs after first operation Pt died soon after of cere bral arteriosclerosis

ADENOLYMPHOMA OF PAROTID GLAND

No	Source	Patient	Age	Sex	Duration of Symptoms	Treatment	Follow-Up
24	Carmichael, Davie, and Stewart Jour Path and Bacteriol 40, 601, 1935		58	F	2½ yrs	Excision	
25	Carmichael, Davie and Stewart Jour Path and Bacteriol, 40, 601 1935		47	M	2 yrs	Excision	
26	Carmichael Davie and Stewart Jour Path and Bacteriol 40, 601 1935		58	M	30 yrs with increase in size during last 3 yrs	Excision	No recurrence after 2 yrs
27	Carmichael Davie and Stewart Jour Path and Bacteriol 40, 601 1935		58	M	10 mos	Excision	No recurrence after 1 yr
28	Carmichael Davie, and Stewart Jour Path and Bacteriol 40, 601, 1935		92	M	15 yrs	Excision	No recurrence after 6 mos
29	Carmichael Davie, and Stewart Jour Path and Bacteriol 40, 601 1935		66	F	3 mos	Excision	
30	Carmichael Davie and Stewart Jour Path and Bacteriol 40, 601 1935		76	F	2½ yrs	Excision	
31	Ssobolew Frankfurt Ztschr f Path 11 462 1912		54	M	5 mos		Letter returned undelivered
32	Ssobolew Frankfurt Ztschr f Path 11, 462 1912		Middle-aged	M			' Malignant in part '
33	Feldman Zentralbl f allg Path u path Anat 27, 25 1916			M	8½ yrs		
34	Nicholson G W Guy's Hosp Rep, 73, 37 1923		60	F	Few mos '	Excision	Patient of Sir R Luce retired Records not available at Guy's Hospital
35	Nicholson G W Guy's Hosp Rep, 73, 37 1923		50	M	1 or 2 yrs	Excision	Guy's Hospital records not available now
36	Stohr Risak Arch f klin Chir 143, 609 1926	Franz Str Pr Nr 734/1925	2½	M	8 wks	Excision	Malignant
37	Letulle Bull de l Assn franc p l'étude du Cancer 16, 380 1927		Adult	M			
38	Bottin Bull de l Assn franc p l etude du Cancer 18, 819 1929		56	M	1 yr		
39	Brachetto-Brian Bol y trab de la Soc de cir de Buenos Aires		57	M	1 yr	Excision	Well No recurrence after 10½ yrs
40	Hamperl Virch Arch f path Anat 282, 724 1931		70	M			
41	Hall E M Arch Path 19 756 1935		48	M	1 yr	Excision	Well No recurrence after 6½ yrs
42	Harris P N Am Jour Path 13, 81 1937		61	M		Excision	Well No recurrence 2 yrs later
43	Harris, P N Am Jour Path 13, 81 1937		62	M	4 yrs	Excision	Well No recurrence 5 yrs later

TABLE IV—(Continued)

No	Source	Patient	Age	Sex	Duration of Symptoms	Treatment	Follow Up
44	Wendel, A Jr Jour Cancer Res 14, 123 1930		56	M	1½ yrs	Excision	No recurrence 10 yrs later Died of heart trouble'
45	Cunningham W F ANNALS OF SURGERY 90, 114 1929	Hist No 6911 Belle vue Hcsp N Y C	16		3 yrs	Excision	Record can't be located
46	Wood D A Am Jour Path 11, 889 1935		37	M			
47	Wood D A Am Jour Path 11, 889 1935		18	M			
48	Wood D A Am Jour Path 11, 889 1935		71	M			

16 PREVIOUSLY UNREPORTED CASES

49	Memorial Hospital* records 1915-1941	B R 57792— 1939	54	M	1 yr	Excision	No recurrence 1 yr 8 mos later Also has reticulum cell lymphosarcoma- tosis
50	Memorial Hospital* records 1915-1941	G E M 49561— 1935	17	M	1 yr	Excision	No recurrence after 1 mo
51	Memorial Hospital* records 1915-1941	I I 53504— 1937	41	M	6 mos	Excision	Fails to respond to follow up requests
52	Memorial Hospital* records 1915-1941	E C 56329— 1938	8½	F	1 yr	Excised Keloid of scar later treated with ra- don bulb	No recurrence after 2 yrs 4 mos
53	Memorial Hospital* records 1915-1941	W K 53265— 1937	51	M	10 mos	Excision	No recurrence after 3 yrs 8 mos
54	Memorial Hospital* records 1915-1941	J L 59329— 1940	53	M	6 mos	Excision	No recurrence after 1 yr
55	Memorial Hospital* records 1915-1941	J L 57840— 1939	64	M	3 mos	Excision followed by x ray	See text Tumor hardly palpable after 1 yr
56	Memorial Hospital* records 1915-1941	E M 60724— 1940	69	M	3 yrs	Excision	No recurrence after 3 mos
57	Memorial Hospital* records 1915-1941	C O 58899— 1940	58	M	3 yrs	Excision	No recurrence after 1 yr 2 mos
58	Memorial Hospital* records 1915-1941	G K 49973— 1935	36	F	1 yr	Excision	No recurrence after 5 yrs 9 mos
59	Oughterson A W * New Haven Hospital	B18276	53	M	3 to 4 yrs	Excision (bilat- eral)	Too recent
60	Stout and Fabro* Presbyterian Hosp N Y C	Hist No 260904 Path No 61427	51	M	1 yr	Excision	No recurrence after 4 yrs
61	Stout and Fabro* Presbyterian Hosp N Y C	Hist No 418878 Path No 54494	55	F	1 yr	Excision, followed by x ray for keloid	No recurrence after 5 yrs

* I am indebted to Drs A W Oughterson, Arthur Purdy Stout, J Alfred Fabro, and Hayes Martin for permission to include the data on these cases

No	Source	Patient	Age	Sex	Duration of Symptoms	Treatment	Follow-Up
62	Stout and Fabro* Presbyterian Hosp N Y C	Surg Path No 14010	54	M	1½ yrs	Biopsy	Died of pneumonia 1 yr after biopsy Tumor had grown 'only slightly
63	Stout and Fabro* Presbyterian Hosp N Y C	Surg Path No 13751	61	M	6 mos	Excision	None
64	Stout and Fabro* Presbyterian Hosp N Y C	Surg Path No 15811				Excision	No recurrence after 2 yrs

Prognosis—From the information at hand, adenolymphoma is a benign tumor (with rare exceptions) which, when adequately excised, usually does not recur.

Added to the 64 cases analyzed above are three others. Although histologically, they differ slightly from the usual picture, they undoubtedly belong to the same group of neoplasms. Clinically, they behave in an identical manner.

CASE REPORTS

Case 1—New Haven Hospital No B7034, Path No 23559. A white male, age 59, was referred to the hospital, July 24, 1940, by Doctor Brown, of Danbury. Eleven months previously a mass appeared in the region of the left parotid gland. This seemed to diminish in size after extraction of a diseased tooth, then renewed its former slow growth. In the two weeks before admission the mass grew more rapidly.

Examination showed a firm, nontender mass behind the angle of the jaw, measuring 2×2.5 cm. There was a tongue-like projection around the ramus of the mandible. There were no other pertinent findings. A "metastatic series" of roentgenograms failed to show any other tumors. RBC 5,500,000, WBC 10,850, with a normal differential distribution. Hemoglobin was 16 Gm. On July 30, 1940, the mass was excised under local novocain anesthesia. At operation no distinct capsule was grossly observed between the parotid gland and the tumor, and the lower portion of the gland was excised, including the neoplasm.

Postoperatively, a small salivary sinus tract drained for about three weeks. This healed quickly. The patient is being followed in the Tumor Clinic. When last seen over a year since the excision, there was no recurrence.

Case 2 †—Mount Sinai Hospital, New York, Path No 18718. A white male, age 53, had had a swelling in the left parotid region for four years. The tumor was completely removed surgically. There was no postoperative radiation. Six months after the excision there was no recurrence.

Case 3 ‡—Mount Sinai Hospital, New York, Path No 18753. A male, age 50, had noted a tumor in the region of the left parotid gland for about two years prior to seeking therapy. The mass was excised, but since the surgeon did not believe all the tumor was removed, he implanted radium as follows: At upper angle of wound, 19.8 mg (1.0 Mm platinum) 11 cm active length for 24 hours. Total 475.2 mg hours. At lower angle of wound, the same factors and dosage. Total 475.2 mg hours. Postoperatively, he was given roentgenotherapy. Dosage 325 r in four divided doses (200 KV, 1 Mm Cu). This case is too recent to report a follow-up.

* I am indebted to Drs. A. W. Oughterson, Arthur Purdy Stout, J. Alfred Fabro, and Hayes Martin for permission to include the data on these cases.

† I am indebted to Drs. Paul Klemperer and John Garlock for permission to report this case.

‡ I wish to thank Drs. Paul Klemperer and Ralph Colp for permission to include this case.

Microscopically, these three tumors are strikingly similar to each other. Like the usual form of adenolymphoma they contain a matrix of lymphoid tissue (Fig 2). In areas, this consists of diffuse lymphocytic infiltration. Elsewhere, there are aggregates resembling germinal centers. In the center



FIG 2—Tumor in Case 1. Compare with Figure 3. (X300)



FIG 3—Lymph node adjacent to parotid gland, Newborn infant. (X200)

of the latter are groups of large cells which resemble epithelioid cells rather than young lymphocytes. Here and there are many small cysts lined with low cylindrical cells with vesicular nuclei. Between the bases of these are small cuboidal cells, irregularly spaced. The cysts contain a pale pink, homogeneous material, cellular debris, and occasionally cholesterol crystals. In addition to the small cysts, and scattered in the lymphoid matrix, are other epithelial cells, singly and in strands. In places the tumor is separated from the parotid gland by a thin fibrous capsule. Elsewhere, there is no capsule and the tumor infiltrates the glandular parenchyma.

Pathologically, all of these tumors resemble that described recently by Fein,⁴ classified by him as lympho-epithelioma.

Histogenesis—The theories concerning the origin of adenolymphomata have been thoroughly presented by Jaffe,⁶ Stout and Kraissl,¹³ Freshman and Kuland,³ Albrecht and Artz,¹ Hamperl,⁵ Waithin,¹⁴ and others. The reader is referred to these authors for a complete discussion.

The presence of parotid ducts and acini within the surrounding lymph nodes has been described by R. Neisse,⁸ and G. W. Nicholson.⁹ Neisse, who studied these structures in fetuses as well as newborn infants, felt that the parotid tissue became included in the lymph nodes as a result of the growth and development of the nodes from small patches of lymphocytes which had previously surrounded the parotid tissue. He found undeveloped parotid structures directly adjacent to lymphocytic tissue in the 9-cm fetuses and lying within the nodes themselves in fetuses measuring 12 cm and larger.

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* I wish to thank Doctor Bunting, particularly, for his help here.

Pathology, Yale School of Medicine, repeated the investigation. They studied the lymph nodes adjacent to the parotid gland in two premature and five full term, stillborn infants. In three of this group small acinar structures and ducts typical of the parotid were found within these lymph nodes (Fig 3). In most instances, these glandular structures were situated in the hilar regions of the nodes (a fact also noted by Neisse and by Nicholson).

From the similarity of the structure of the three tumors described above to that of this common finding in newborn infants, it seems probable that such tumors have arisen from the subsequent growth of such parotid tubules and acini as have been included within lymph nodes.

CONCLUSIONS

Adenolymphoma of the parotid region is an unusual salivary gland tumor. It probably comprises considerably less than 10 per cent of all parotid tumors. Were complete figures known, this ratio would presumably fall lower. It occurs at all ages, but predominantly in the fifth, sixth, and seventh decades. The life history is that of a slow growing tumor, which is relatively asymptomatic. The tumor is usually present for many months before attention is sought. It occurs five times oftener in men than in women. Surgical excision is the treatment of choice. Since the capsule is not always complete, the tumor should be meticulously dissected out, rather than enucleated. When completely excised, the tumor rarely has been known to recur. Histologically, it is benign. A discussion is appended concerning the possible histogenesis of adenolymphomata. Three cases are reported of a clinically identical and histologically similar tumor, which the author believes belong to the same group.

BIBLIOGRAPHY

- ¹ Albrecht and Aitz. Frankfurt Ztschr f Path, **282**, 724, 1910.
- ² Carmichael, R, Davie, T B, and Stewart, M J. Adenolymphoma of Salivary Glands. Jour Path and Bact, **40**, 601-615, 1925.
- ³ Freshman, A W, and Kurland, Stanley K. Cystadenoma Lymphomatosum. Am Jour Clin Path, **8**, 422-430, 1938.
- ⁴ Fein, M J. Lympho-epithelioma of the Parotid Gland. Am Jour Cancer, **40**, 434-440, 1940.
- ⁵ Hamperl, H. Virchow's Arch f Path Anat, **282**, 724, 1931.
- ⁶ Jaffe, R H. Adenolymphoma (Onkocytoma) of Parotid Gland. Am Jour Cancer, **16**, 1415-1423, 1932.
- ⁷ Klemperei, Paul. Personal communication.
- ⁸ Neisse, R. Über den Einschluss von Parotislapchen in Lymphknoten. Anat Hefte, **10**, 289, 1898.
- ⁹ Nicholson, G W. Studies on Tumor Formation. Guy's Hospital Reports, **2**, 333, 1922.
- ¹⁰ Niño, F L. Cistoadenolinfomas papilíferos del cuello. Bol de clin quir, univ de Buenos Aires, **16**, 271, 1940.
- ¹¹ Ssobolew, L W. Frankfurt Ztschr f Path, **11**, 462, 1912.
- ¹² Stohr, Fritz, and Risak, Erwin. Arch f klin Chir, **143**, 609, 1926.
- ¹³ Stout, Arthur Purdy, and Kraissl, C J. Orbital Inclusion Cysts and Cysto-adenomas of Parotid Salivary Glands. Personal communication, and Arch Surg, **26**, 485-499, 1933.
- ¹⁴ Warthin, A S. Papillary Cystadenoma Lymphomatosum. Rare Teratoid of Parotid Region. Jour Cancer Res, **13**, 116-125, 1929.
- ¹⁵ Weller, Carl. Personal communication.

ADRENALIN-PRODUCING PHEOCHROMOCYTOMA OF THE ADRENAL ASSOCIATED WITH HYPERTENSION

REPORT OF THREE CASES

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THE TERM PHEOCHROMOCYTOMA is restricted to-day to those tumors that arise from the adrenal medulla, whereas the term paraganglioma connotes a tumor that originates in the chromaffin system exclusive of the adrenal gland. Pheochromocytomata are characterized chiefly by the markedly increased production of adrenalin, which, according to Ewing,¹ occurs only in the benign forms. These tumors are usually benign and the diagnosis of malignancy can only be made on histologic examination of the tumor and not on the clinical findings. Surgical removal of the tumor usually results in relief of the hypertension.

Grossly, these tumors are moderately firm, and vary in size from that of a pinhead to the size of a fetal head and have been reported to weigh up to 2,000 Gm. Microscopically, these tumors form small groups of cells or show a diffuse growth of polygonal, oval, or round cells. Giant cells are usually present, may be either mononuclear or multinuclear, and often resemble ganglion cells. The stroma which is fibrillar and forms narrow trabeculae contain numerous blood vessels. Hemorrhage, necrosis, and cystic degeneration frequently occur.

In a review of the literature of pheochromocytomata, Brunschwig and Humphreys² collected 103 cases up to 1939. Since then, ten additional cases have been reported. We wish to report three cases of adrenalin-producing pheochromocytoma of the adrenal, from a series of 14,437 consecutive autopsies performed at the Cook County Hospital, from 1929 to March, 1941, inclusive. Of the total group reported to date, there have been 18 cases that have come to surgery, and in those that survived there was a marked permanent drop in blood pressure. A biologic assay of the tumor was performed in only 13 cases from both surgical and autopsy sources. In some instances the assay was qualitative, but in the majority it was quantitative. In one case the authors were able to demonstrate the presence of an increased amount of adrenalin in the blood during an attack.³ The adrenalin content of the tumors examined has varied from 1 to 40 mg. per Gm. of tumor tissue. One of our cases contained 4.15 mg. of adrenalin per Gm. of tissue, while, in another, qualitative tests, only, were performed.

The majority of the cases of pheochromocytoma have been encountered in necropsy material, and it is only since 1929, following the report of Rabin,⁴ that clinicians have made the diagnosis during life. The clinical diagnosis is

usually made on the basis of paroxysmal hypertension, and some of the accompanying symptoms and findings such as glycosuria, vasomotor pallor followed by flushing, headache, nausea, and vomiting, dyspnea, feeling of suffocation, pulmonary edema, and great susceptibility to surgical shock, even during minor surgical procedures. Tachycardia may also be present, although, with the rise in blood pressure, the pulse may become slow and bounding.

In view of the above discussion, it might be well to mention that there are cases of paroxysmal hypertension which have been operated upon with the diagnosis of pheochromocytoma of the adrenal when, at operation, no tumor was found. Recently, one of us (J. D. K.) saw a patient, a female, age 38, operated upon for a suspected pheochromocytoma. Examination of the surgically removed tumor (Fig. 9) revealed a cyst of the adrenal which, when assayed, contained no adrenalin. Removal of the tumor has produced no fall in blood pressure. One year after operation the blood pressure has varied from 190 to 210 systolic and 60 to 90 diastolic.

CASE REPORTS

Case 1—White, male, age 28, entered the Cook County Hospital, December 15, 1940, in a comatose condition. The history was elicited from the mother, who stated that the onset was characterized by a severe headache that started two days before admission, and lasted through the following day. On the day following the onset, he vomited twice and felt better. That night he lapsed into coma. A diagnosis of meningitis was made, and hospitalization advised. The mother stated that the patient had been perfectly well before the acute episode, with the exception of his having had measles in childhood. He had, also, had an operation for congenital cataract, which had resulted in an improvement in his vision.

Physical examination revealed a comatose, white male who was very restless, and who was breathing stertorously. Temperature 104.2° F., pulse 200, blood pressure 230/70. The neck showed a slight rigidity. There was a systolic murmur at the apex. No râles were heard in the lungs. The only other findings of significance were positive Kernig and Brudzinski signs. The spinal fluid was under slightly increased pressure, and was turbid. The Pandy test was 4 plus, the cell count showed 1,090 cells, all polymorphonuclear leukocytes, and on smear, pneumococci, Type 18 were seen. The impression was that the patient had a Type 18 pneumococcic meningitis and an auricular tachycardia. The patient was given sodium sulfapyridine and 360,000 units of pneumococcic antiserum, intravenously. In spite of this therapy his course was rapidly downhill, and the patient expired 15 hours after admission to the hospital.

Autopsy—The body was that of a well-developed, well-nourished white male. The left pupil was larger than the right. The pleural cavities were free. The pericardial sac contained 20 cc. of a clear straw-colored fluid. The heart weighed 520 Gm. The myocardium was very firm and light brown-red. The wall of the left ventricle measured 22 Mm. in thickness, and the right ventricle was 5 Mm. thick. The aorta and the bases of the leaflets of both the aortic and mitral valves showed numerous fatty and hyaline plaques. Both coronary arteries showed a moderate sclerosis and a narrowing of the lumina. The lungs revealed a hemorrhagic bronchopneumonia in all the lobes. The thyroid weighed 12 Gm., and was rich in colloid. The liver was enlarged and weighed 2020 Gm. The spleen weighed 55 Gm. and showed a marked infectious softening. The pancreas weighed 85 Gm. and was soft. The kidneys together, weighed 350 Gm. and showed a marked congestion. The brain was swollen and on the surface especially over the cerebellum, there were small accumulations of a greenish purulent material.

The left adrenal weighed 73 Gm (Fig 1), and was moderately firm. On the surface along one edge there were islands of compressed cortical tissue. For the most part, the mass was encapsulated, firm, and, on section, measured 85x55x40 Mm. The sectioned surface of the mass appeared light grayish-brown. At the periphery it was slightly lighter, while the central portion was occupied by a 20x25 Mm light yellow-green translucent area. Fixation of a portion of the tumor in potassium bichromate solution caused the surface to turn deep brown. The right adrenal weighed 10 Gm, and appeared normal.

Microscopic Examination—This revealed the tumor to be composed of large polygonal cells arranged in alveoli. The cells contained oval to round nuclei, in which were included a finely granular chromatin (Fig 2). In the cytoplasm, particularly in the sections previously fixed in chromate, a fine reddish-brown pigment was present. The nuclei, for the most part, were small, however, many were very large, occasionally

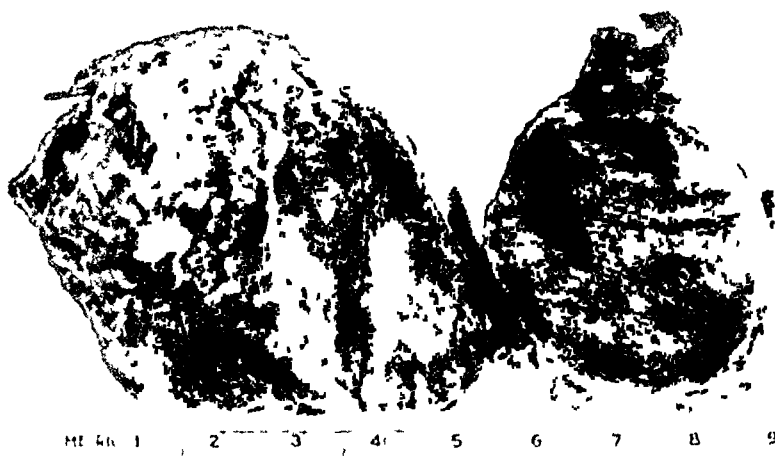


FIG 1.—Case 1. Photograph shows the large pheochromocytoma in the left adrenal. Note the compressed, intact adrenal tissue in the periphery.

of bizarre shape or multinucleated (Fig 3). No mitotic figures were seen. Mallory's stain revealed fine strands of connective tissue between the cells, and the alveoli were separated by narrow trabeculae that often contained blood vessels (Fig 4). Throughout the tumor, but chiefly in the central portion there were extravasations of blood and areas of cystic degeneration. At the periphery of the tumor there was a narrow rim of intact but compressed cortex. Several islands of cortical cells were isolated beneath the capsule of the tumor (Fig 5).

When stained with Sudan III, little fat was seen, and what was present was in the form of coarse fat droplets.

Anatomic Diagnosis—Pneumococcal meningitis (Type 18), pheochromocytoma of the left adrenal, marked hypertrophy of the heart, marked arteriosclerosis of the coronary arteries, the aorta and cerebral vessels, hemorrhagic bronchopneumonia of both lungs, marked fatty changes of the liver and passive congestion of the kidneys.

Bio-assay of Adrenalin Content in the Tumor—Eight grams of the adrenal tumor were submitted to Dr. H. A. McGuigan, of the Department of Pharmacology of the University of Illinois Medical School. The tissue was ground up and extracted with 50 cc of N/10 hydrochloric acid. It was placed in the icebox for 24 hours and re-extracted with 50 cc N/10 hydrochloric acid, filtered and neutralized with sodium carbonate and made up to 500 cc. A male dog, that weighed 12.3 Kg was anesthetized with nembutal. When 0.6 cc of the extract was injected intravenously, a rise in blood

PHEOCHROMOCYTOMA OF ADRENAL

pressure, equal to that produced by the injection of 1 cc of a 1:25,000 solution of adrenalin, was obtained (Graph 1). Eight grams of tumor yielded 33.2 mg of adrenalin, and the entire tumor yielded approximately 303 mg of adrenalin, or 0.31 per cent.

Case 2—White, male, age 53, was admitted to Cook County Hospital, November, 1934, in coma. The temperature was 103.6° F, blood pressure 230/170. No history was available except for a roentgenologic report in his pocket, which stated that the

FIG 2

FIG 3

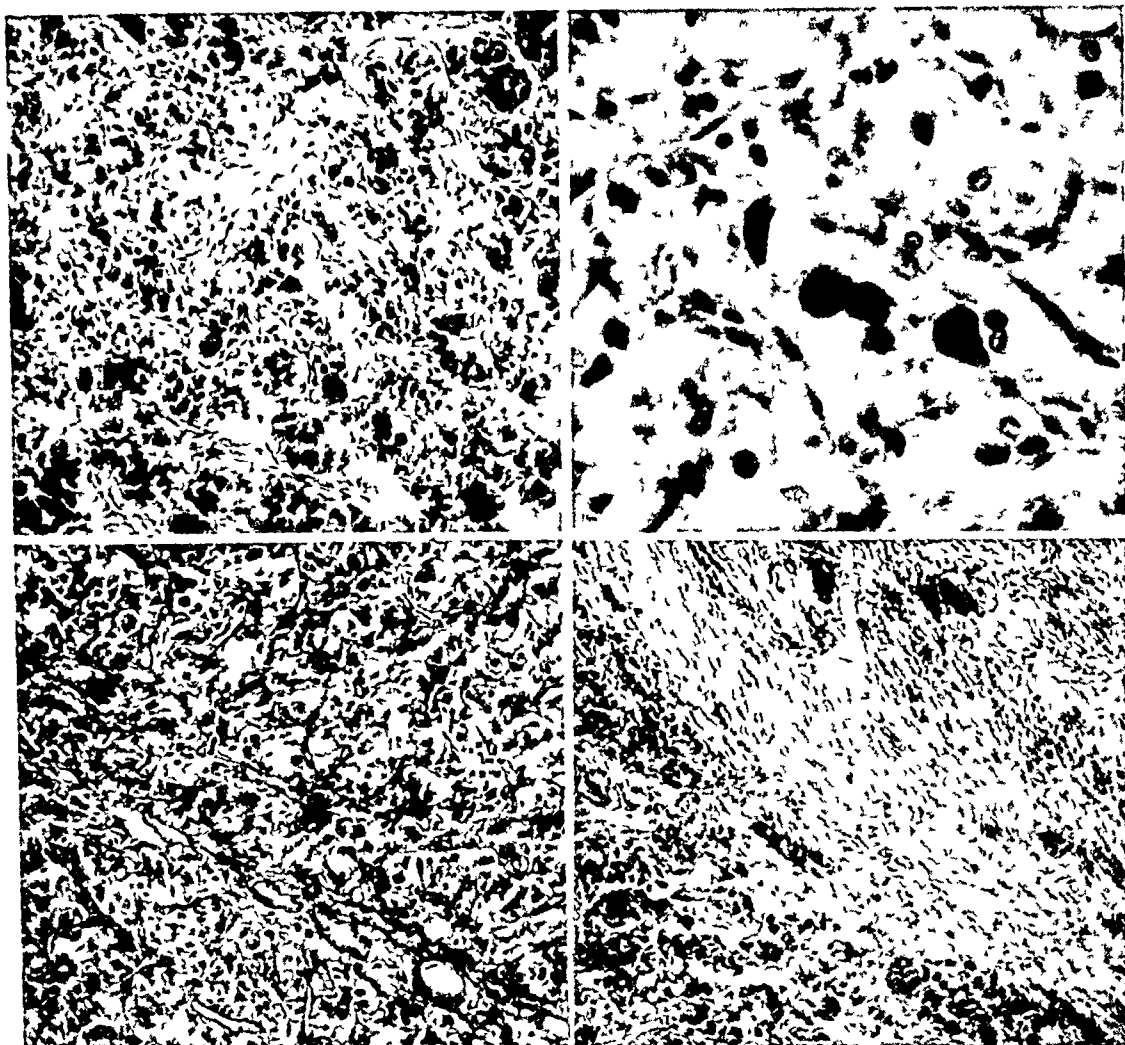


FIG 4

FIG 5

FIG 2—Case 1. Low power magnification showing the alveolar arrangement of the cells.

FIG 3—Case 1. High power magnification. Note the bizarre shaped giant cells resembling ganglion cells.

FIG 4—Case 1. Photomicrograph showing the fine trabeculae between the groups of cells (Mallory's phosphotungstic, hematoxylin).

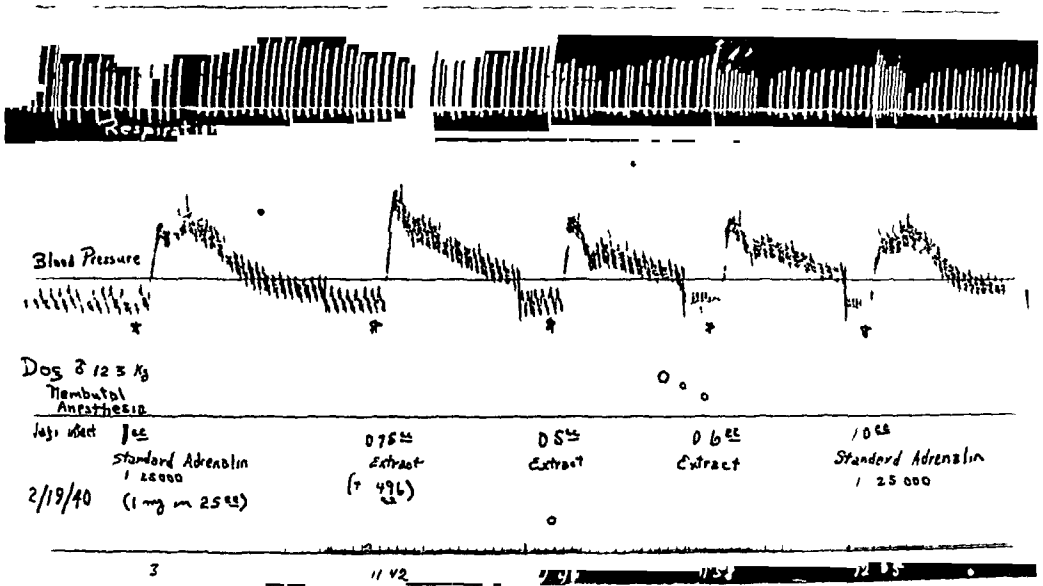
FIG 5—Case 1. Photomicrograph showing the capsule about the tumor, with islands of adrenal tissue in the periphery.

patient may have had a tumor of the lung. He was having Cheyne-Stoke's respirations, and before the examination could be completed, the patient expired.

Necropsy—This disclosed a spontaneous hemorrhage in the right cerebellar hemisphere as the immediate cause of death. The left adrenal was transformed into a mass 10x8.5x8 cm (Fig 6). It was encapsulated and moderately firm. On section, it was light brown, and contained several cystic areas that measured up to 2.5 cm in diameter. Histologically, this tumor resembled the one previously described (Case 1), except that the trabeculae were coarser and often isolated small groups of cells (Fig 7). In addition to the above findings, there were many pinhead, up to 2 mm in diameter, sub-

cutaneous nodules and areas of pale brown pigmentation over the trunk, neck, and extremities. There was also a goose egg-sized, semifirm mass in the right third interspace, which was attached to the intercostal nerve. There was, also, a small, solitary neurofibroma in the submucosa of the stomach.

Anatomic Diagnosis—Massive, spontaneous cerebellar hemorrhage, benign pheochromocytoma of the left adrenal, multiple neurofibromata in the skin, single neurofibroma in the stomach, and in the right third intercostal space.



GRAPH 1—Case 1. Photograph of the tracing showing the effects of injecting an extract of tumor tissue into a dog. Note the prompt rise in blood pressure.

Case 3—Previously reported by Ford K. Hick.⁵ White female, age 64, was brought to Cook County Hospital in a stuporous state, and died a few hours later. It was learned from a son that the patient had slept much of the time during the day for the past few weeks.

Physical examination disclosed an obese, white female, blood pressure 180/105. The pupils were unequal. *Clinical Diagnosis*: Cerebral hemorrhage.

Autopsy—The essential anatomic findings were a pea-sized aneurysm of the anterior communicating cerebral artery, with rupture, and severe subarachnoid hemorrhage. Attached to the left adrenal gland was an encapsulated soft egg-shaped mass, measuring 4×2×2 cm (Fig. 8). Histologically, this tumor resembled the two preceding cases (Cases 1 and 2).

Anatomic Diagnosis—Ruptured aneurysm of the anterior communicating cerebral artery, with extensive intra- and extrameningeal hemorrhage at the base of the brain, pheochromocytoma in the region of the left suprarenal gland.

When an extract of a gram of tumor tissue was injected into a dog, it produced a marked rise in blood pressure. No quantitative determination of the adrenalin content of the tumor was made.

COMMENT—Our first case is unique in that it occurred in a young male, age 28, who, at autopsy, showed the effects of a long-standing hypertension, such as the marked enlargement of the heart and arteriosclerosis, but without pathologic changes in the kidneys. As far as could be learned from the past history, there was no evidence that the patient may have had a paroxys-

mal type of hypertension. Thus, one might suggest that the secretion of adrenalin from the tumor was continuous rather than intermittent.

The second case is one of the few reported in which there is a coincident neurofibromatosis. In 1938 Bienen, Konzett and Nagl⁶ reviewed the literature and, out of 64 cases of pheochromocytoma, reported they were able



FIG 6—Case 2. Photograph of a pheochromocytoma of the left adrenal. Note areas of cystic degeneration.



FIG 7—Case 2. Photograph showing the tumor attached to the left adrenal, with central, cystic degeneration.

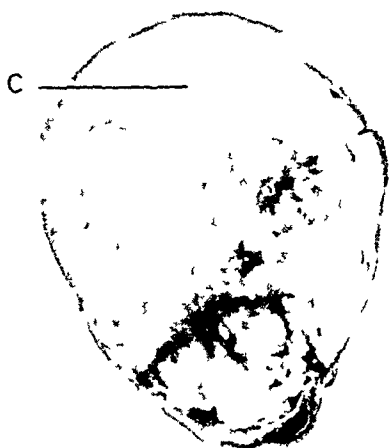


FIG 8—Case 3. Photograph showing a large cyst of the adrenal. Note (A) islands of adrenal tissue on the surface of the tumor. (C) Plaques of calcium lining the thin walled cyst. This patient had a paroxysmal type of hypertension which was unrelieved following surgical removal of the tumor.

to find only eight cases in which these two pathologic processes occurred concomitantly. The third case was peculiar in that the tumor was outside but attached to the adrenal. Hick⁷ believed that the tumor had its origin in the medulla, and, as it grew, it became separated from the adrenal.

Two of the three cases here presented were males, and the third was a female. The age incidence ranged from 28 to 64 years. The majority of cases reported occurred in the third and fourth decades, although one of the cases recorded was in a 12-year-old girl. The majority of these tumors

are unilateral, however, Brunschwig and Humphreys² noted 13 instances of bilateral involvement

SUMMARY

Three cases of pheochromocytoma of the adrenal are here presented. One of these tumors was situated outside of the adrenal, but was attached to it. Two occurred in males (28 and 53 years of age), and the third, in a female (age 64).

All three tumors were benign, and were incidental findings at necropsy.

Hypertension was present in all three cases and the systolic pressures ranged from 180 to 230 mm Hg.

Two of the three cases (Cases 1 and 3), when assayed, revealed an adrenalin-producing substance. In Case 1, 73.0 Gm of tumor tissue yielded approximately 303 mg of adrenalin.

Arteriosclerosis was a prominent feature in all the cases, and the heart was hypertrophied in all.

Neurofibromatosis may be associated with pheochromocytoma, as it was in one of the cases.

A case of a calcified cyst of the adrenal in a woman, age 38, who had developed a sudden hypertension, and was not relieved of her high blood pressure subsequent to surgical extirpation of the tumor, is cited.

A total of 116 cases of pheochromocytoma of the adrenal, from both surgical and necropsy sources, have thus far been reported.

REFERENCES

- ¹ Ewing, James. Neoplastic Diseases. 4th ed., Saunders and Co., p. 838, 1940.
- ² Brunschwig, A., and Humphreys, E. JAMA, 115, 355-357, 1940.
- ³ Beer, E., King, F. H., Prinzmetal, M. ANNALS OF SURGERY, 106, 85-91, 1937.
- ⁴ Rabin, C. B. Arch Path., 7, 288, 1929.
- ⁵ Hick, F. K. Arch Path., 15, 665-674, 1933.
- ⁶ Brenner, F., Konzett, H., Nagl, F. Munchen med Wchnschr., 85, 914-916, 1938.
- ⁷ Evans, V. L. Jour Lab and Clin Med., 22, 1117-1120, 1937.

PHEOCHROMOCYTOMA WITH HYPERMETABOLISM

REPORT OF TWO CASES

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THE CLINICAL SYNDROME associated with pheochromocytoma tumors of the adrenal medulla has come to be a well recognized entity and a number of cases have been reported, some of which have been relieved by surgical removal of the tumor. Although paroxysmal hypertension has frequently been noted, it is not a *sine qua non* in the diagnosis. In our two cases persistent hypertension developed. Variations in blood pressure were present early in the course of observation in the first case and these persisted and were superimposed upon the constant hypertension in the second case. One of our cases was correctly diagnosed before operation and was cured by surgical removal of the tumor, while the second is from our records and was diagnosed at autopsy, having been considered clinically to be hyperthyroidism. Hypermetabolism was an outstanding feature in both cases.

Until the past decade, the vast majority of these tumors were found at autopsy and reported by pathologists. Brunschwig and Humphreys¹ found 103 cases in the literature to 1940. These were mostly found at autopsy. McKenzie and MacEachern² presented an excellent paper in 1938, at which time they had collected 20 cases treated surgically. Since that time several additional surgical cases have been reported. Although the tumor is still uncommon, it is being recognized and properly treated much more frequently now than it was previously.

CASE REPORTS

Case 1—A 19-year-old girl student was referred to one of us (E P McC) on June 12, 1939, with the following history. On December 24, 1937, she was knocked down by an automobile. She was not badly hurt, although roentgenologic examination the following day disclosed three fractured ribs on the right side. During the following year she tired readily, and was not strong enough to attend school, her illness confining her to bed for a week or two at a time during 1938. There was some loss of weight, although she ate and slept well. The family physician found that she had some hypertension. She then consulted another physician who checked her blood pressure very carefully and told her that there was absolutely no elevation and that she should forget about it. The family physician, not being satisfied with this urged consultation with a third physician, who found a definite hypertension. This experience caused the family to lose faith in the second physician who was an exceedingly capable man and this was restored only after it was explained that they all were correct.

During the six months preceding our examination, in addition to weakness, she complained of "spells" which occurred 15 to 20 times a day. In a typical attack the patient first experienced a sense of intense heat occurring first over the face, and then extending over the entire body. This was occasionally associated with momentary dizziness and faintness. Almost immediately after the sensation of heat a profuse, drenching

perspiration began which also started on the face and spread from there over the body. The hands and feet did not participate in this hyperhydrosis and usually felt cold and clammy. With the spells she always experienced palpitation of the heart with increased precordial activity, and could feel the pounding in the abdominal aorta. With these attacks she felt trembly and often her whole body shook. The spells lasted a few minutes, and when frequent, one merged into the next. They occurred at any time of the day or night and were never precipitated in any constant manner, often occurring when she was apparently at complete rest. Between spells there was weakness but no other outstanding symptoms.

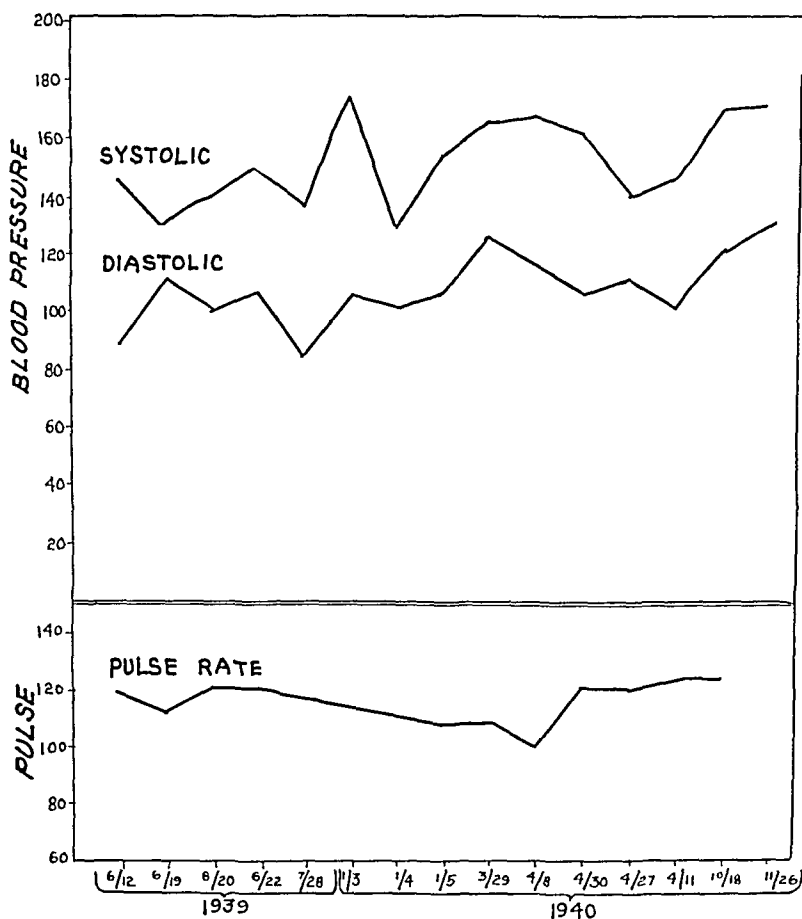


CHART 1

Physical Examination—The patient was an asthenic, tired looking young woman. Weight 111 pounds (50.5 Kg), pulse 120, blood pressure 152/100. The eyes were normal and there was no exophthalmos. The thyroid was palpable but not enlarged. The chest and lungs were normal. A medium-grade digital tremor was present. Complete neurologic examination showed no other abnormalities.

Laboratory Data—Urinalysis showed the p_H of the urine to be 5.2, the specific gravity 1.020, with a trace of albumin, and no sugar. Microscopic examination showed rare red blood cells and one to two white blood cells per high power field. The fasting blood sugar was 95 mg, blood urea 30 mg, and cholesterol 139 mg per cent. Wassermann and Kahn tests negative. On June 19, 1939, the urea clearance test showed 147 per cent the first hour, 125 per cent the second hour. On December 9, 1940, the urea clearance test showed 140 per cent the first hour, 130 per cent the second hour, and the

PHEOCHROMOCYTOMA

blood urea was 33 mg per 100 cc The glucose tolerance, using 100 Gm of glucose by the oral single dose method, October 11, 1940, showed the following blood sugar levels

Hour	Fasting	½	1	2	3	4
Blood sugar	128	267	254	75	45	76

Although diabetes was not present, it is interesting to compare this with the same test done postoperatively January 31, 1941 There had been a definite fall in blood sugar levels at that time The test was as follows

Hour	Fasting	½	1	2	3	4
Blood sugar	88	168	168	108	49	72

Although it was not suspected that adenal cortical sex hormones would be at abnormal levels, these were determined The androgens, by the capon comb-growth method of McCullagh and McLin,⁴ were 11 IU in a 24-hour specimen Seventeen-ketosteroids,

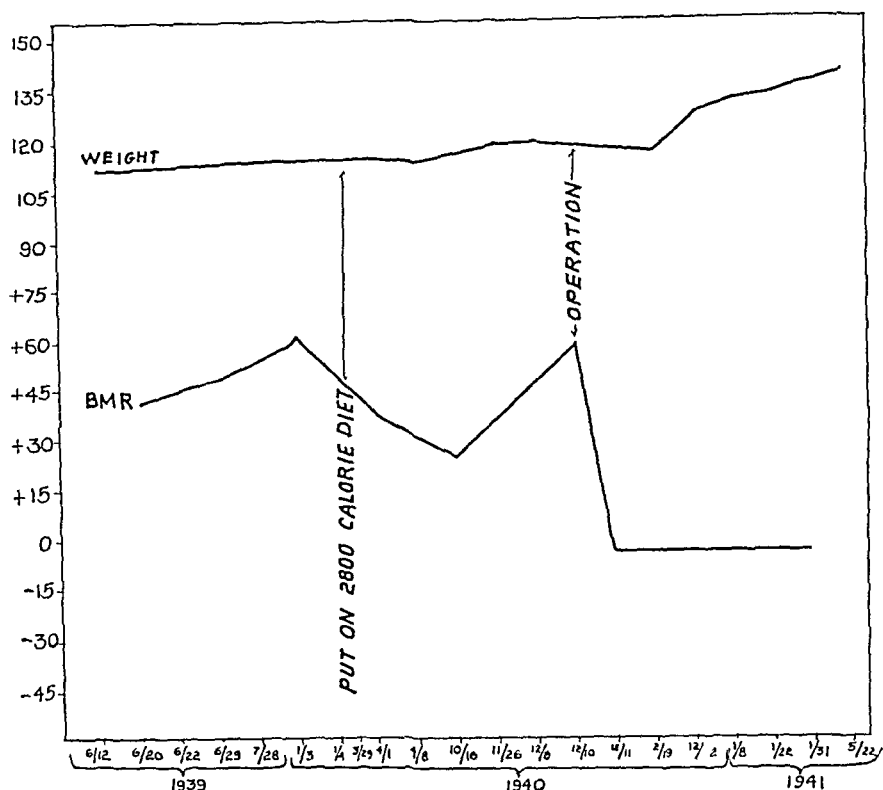


CHART 2

estimated by the electric colorimeter by a modification of the Callow method, showed 28 colorimetric units, which is normal

Following the first examination and reports, the impression was either neurocirculatory asthenia or adrenal sympathetic syndrome, as in pheochromocytoma

For further investigation, she was referred to the Department of Urology, June 23, 1939 Cystoscopic examination revealed a normal bladder Ureteral catheters were passed and separate kidney urines were normal The bilateral pyelogram showed normal kidney pelvis and neither kidney was displaced No tumor shadow could be seen in the suprarenal area Perirenal air injection was suggested and carried out, June 28, 1939 However, before the requisite amount of air could be injected, the patient became dyspneic, suffered mild collapse, and the injection was discontinued Roentgenograms made at the time and again the following day were of no assistance in diagnosis, as there was insufficient air in the tissues

We were, therefore, unable to establish a definite diagnosis of adrenal tumor, so the

* Normal for women approximately 10 to 50 international units

patient continued under the observation of one of us (E P McC) She continued to have the spells of weakness, profuse sweating, and fatigue, although there was little change in her general appearance or condition for the next 18 months. The blood pressure, although variable, was elevated for the most part, and she was never observed to have what we considered to be true paroxysms of hypertension (Chart 1). Even with her spells, the blood pressure was recorded no higher than occasionally at other times. There was persistent tachycardia, and repeated determinations of the basal metabolic rate showed a constant hypermetabolism (Chart 2). In spite of this she never was considered to be a case of hyperthyroidism and the surgical consultant shared this opinion.

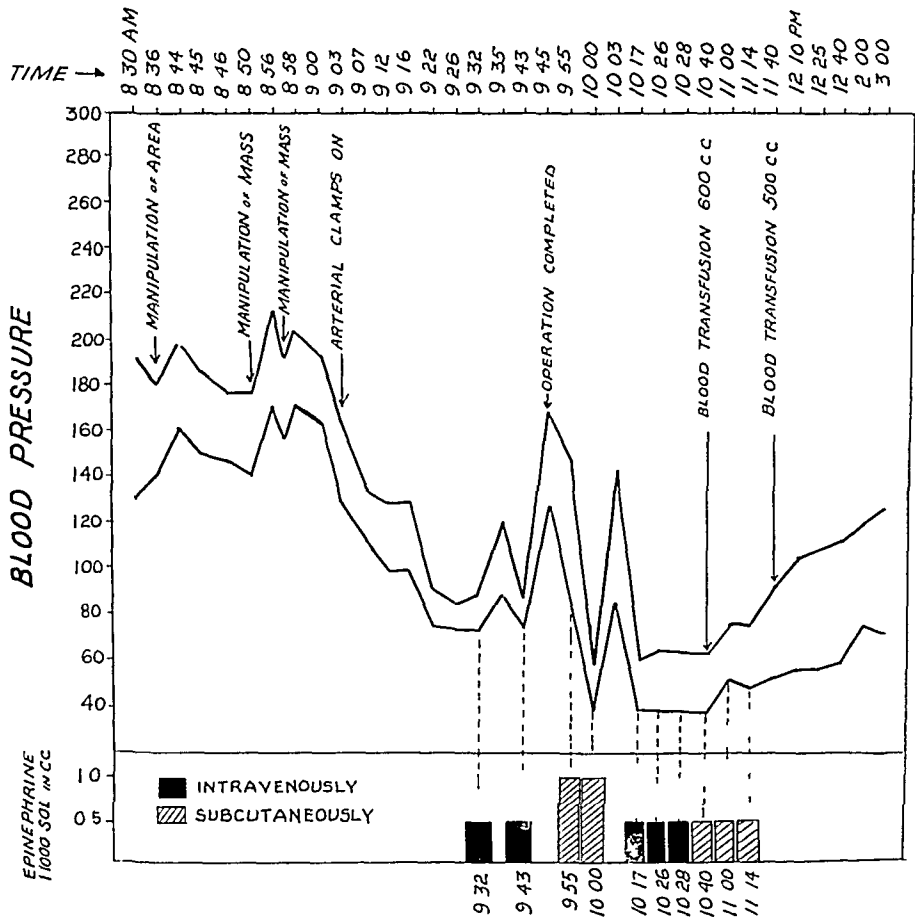


CHART 3

Throughout this period of observation the clinical diagnosis was probable pheochromocytoma. In October, 1940, an intravenous urogram was made, but we were still unable to demonstrate any displacement of either kidney and there was no tumor shadow in either suprarenal area. On clinical evidence, however, adrenal exploration was advised, and the patient returned for operation in December, 1940.

The patient was prepared for bilateral adrenal exploration after the technic described by Young⁴. We decided to explore the right side first because these tumors are more prevalent on the right side, and also because the right kidney was lower, which made it seem improbable that the tumor was on the left side.

Even before seeing the tumor we were sure of its presence. Constant blood pressure determinations were made during the operation and manipulation in the suprarenal area was followed by rapid rise of systolic and diastolic pressures to alarming levels (Chart 3). When the tumor was exposed, touching it produced extreme elevation of the blood

pressure as high as 170 Mm diastolic. As dissection of the tumor proceeded we could see that it was separate from the adrenal gland, which was left intact.

As soon as the blood supply to the tumor was interrupted, the blood pressure dropped precipitously. A plasma transfusion was begun and also the administration of epinephrine, which it was necessary to use in repeated, rather large doses to support the circulation. Doses of 0.5-1.0 cc of 1/1000 solution were given intravenously at intervals of a few minutes whenever the systolic pressure fell below 90 Mm, a total of 60 cc being administered within three hours following severance of the blood supply to the mass. It was interesting to observe that after the first few doses the drug apparently lost its effectiveness and its administration no longer resulted in a significant rise of pressure. Immediately upon completion of the operation, the patient's condition was quite satisfactory.

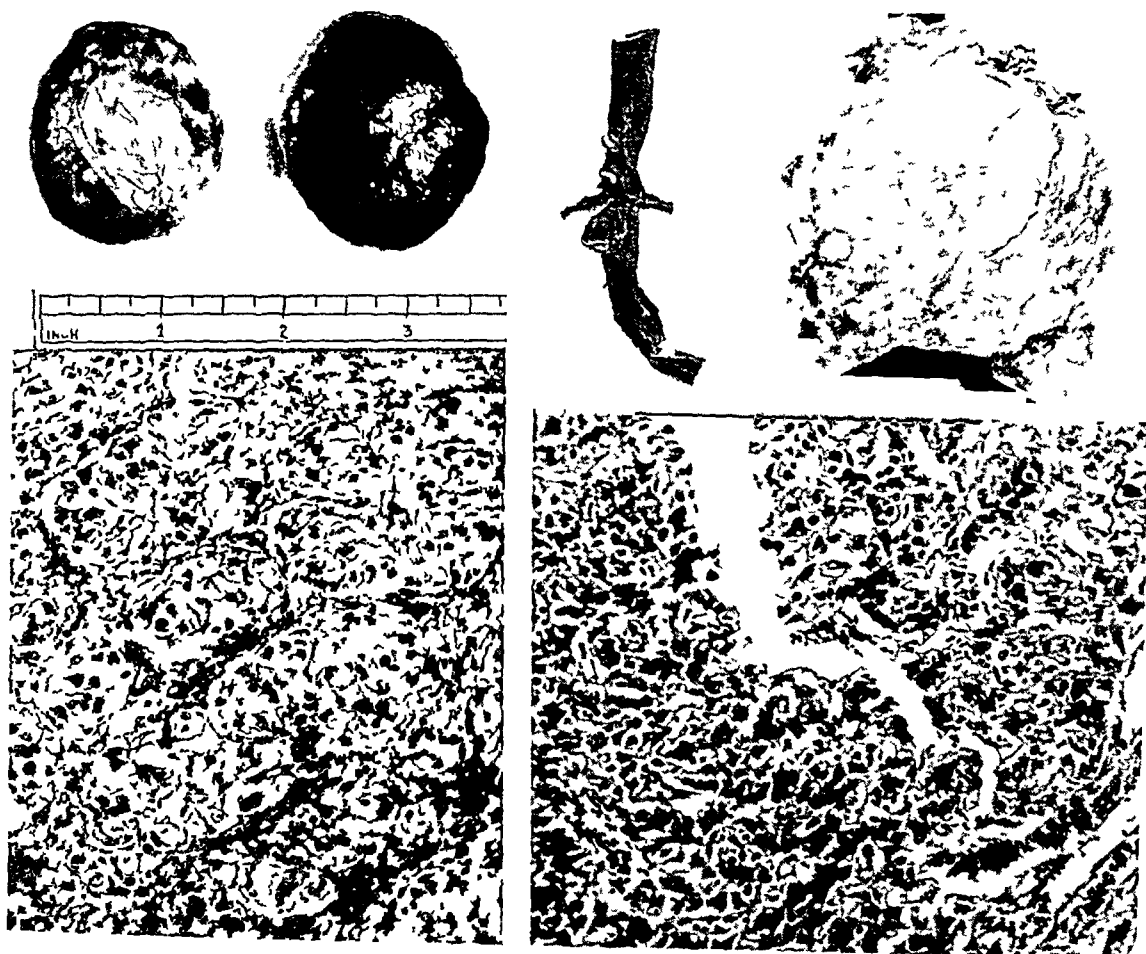


FIG 1

FIG 2

Figs 1 and 2—The gross and microscopic appearance of the tumors in Cases 1 and 2, respectively, are shown. The cells of the tumors in each simulate those seen in normal adrenal medulla.

although the blood pressure had not yet risen. Within the next four hours, the patient was given two transfusions of whole blood containing 500 and 600 cc, respectively. By midafternoon of the day of operation the blood pressure had returned to normal, and remained so throughout the remainder of her convalescence.

The great value of transfusion of blood or plasma during and following operation in these cases should be emphasized.

Pathologic Examination—Dr Allen Graham: "The specimen consists of a tumor mass (Fig 1) removed from the right adrenal, it weighs 35 Gm and measures 5.5x4.3x3.5 cm. It is entirely encapsulated, has a fairly uniform surface, is firm, elastic, and, on section, has a uniform, bulging, homogeneous, yellowish-brown surface. The entire tumor has the color and consistency of adrenal medullary tissue.

"Histologic sections show a very cellular type of tumor consisting of very large irregular cells having an abundance of cytoplasm in which there are many granules. The cells correspond in type to those of the adrenal medulla. The tumor is highly vascularized and has a reticulated stroma." *Pathologic Diagnosis*—Pheochromocytoma of the right adrenal.

The patient had an uneventful convalescence and was permitted to leave the hospital on the eleventh day following operation. She has remained entirely well and reported for observation six months postoperatively, feeling well and having gained some 20 pounds in weight. She has been completely relieved of her attacks and the blood pressure has remained at normal levels, the highest postoperative determination being 130 Mm systolic and 70 Mm diastolic.

The urea clearance test eight months postoperatively showed 85 per cent clearance in each of two hours. The basal metabolic rates were -4 and -6 per cent. The blood pressure was 124 Mm systolic and 70 Mm diastolic. At this time she reported that her weight had decreased ten pounds without any effort or dietary restrictions, the appetite apparently having adjusted itself automatically to metabolic needs.

COMMENT—Several interesting features of this case bear special comment. Although the blood pressure was variable, this variability was never shown to bear any relationship to her symptoms, for it was repeatedly found to be normal during an attack of sweating, and on several occasions was found to be high when she was feeling well and no attack was present. Of interest also is the upward trend of the blood pressure during the one and one-half years she was under observation before operation (Chart 1). At first, normal readings were occasionally obtained, later, the blood pressure was constantly elevated, much as is seen in essential hypertension. The eyegrounds were examined by the ophthalmologist and were reported to show the changes of essential hypertension, Grades I to II. Attempts were made to reproduce her attacks or aggravate her hypertension by manipulation of the adrenal areas and by bending exercises, but these failed. The rapid flow of blood through the tissues is shown here, as in the second case, to be reported, by the very high urea clearance tests which reveal the result of excessive circulation through a normal kidney. This test, in our opinion, is of particular interest in considering the origin of the hypertension.

The spells of weakness and extreme sweating which formed the chief complaints in this case were at first suspected of being of hypoglycemic origin, but no hypoglycemia was found. Neither did she develop any clinical evidence of diabetes. It is noteworthy, nevertheless, that there was a shift in tolerance to glucose which was apparently brought about following the removal of the tumor, showing that some strain on the glucose metabolism did exist.

Throughout the course of the patient's illness she did not exhibit the marked general redness of the skin which is described in Case 2, but her hands did show, on all occasions, a peculiar redness in the same type of glove distribution in which cyanosis appears in neurocirculatory asthenia.

The hypermetabolism is especially worthy of comment. As seen in Chart 2, repeated preoperative determinations of the basal metabolism showed consistent and pronounced elevations. Associated with this the patient had experienced a marked stimulation of her appetite and she was able to maintain

her weight by following a diet approximating 2,800 calories per day. The finding of a rather severe hypermetabolism, naturally, brought the possibility of hyperthyroidism to mind. We felt that this could be excluded by the absence of the typical appearance of hyperthyroidism and of thyroid enlargement and exophthalmos, also a therapeutic trial with Lugol's solution did not alter her clinical state nor affect her basal metabolism. Finally, the proof that the hypermetabolism in this instance was primarily due to the adrenal tumor is produced by the complete return of the metabolic rate to normal after the removal of the mass. Here, then, is hypermetabolism not of thyroid origin, yet this and the following case emphasize the closeness with which pheochromocytoma may simulate hyperthyroidism.

Following operation this patient presented an unusual complaint of cold intolerance. If a cold breeze struck her she would shake perceptibly and on one occasion the shivering continued for most of an hour. This has gradually improved until, eight months postoperatively, it was scarcely noticeable. The only apparent explanation for this is that there was pronounced vasomotor and pilomotor instability from which she required considerable time to recover.

Case 2—A young married man, age 28, entered the hospital in November, 1937, complaining of a "run-down condition." His symptoms were of recent onset, and for the preceding two weeks he had had little energy, felt nervous, generally weak, and had a tremor of his hands. The symptoms became so severe that he was forced to stop working, and three days before admission he became markedly exhausted. In spite of a fair appetite during the preceding year, he had lost 28 pounds in weight.

For a year the patient had experienced increased frequency of urination and during the past four months this had become more pronounced. He was forced to void almost every hour during the day and four to six times at night. This severe frequency was unaccompanied by any associated symptoms of burning or dysuria, and he seemed to pass a normal amount of urine at each voiding.

Physical Examination—The patient was a well-developed man, who had an extremely red face, and a very red, deeply fissured tongue. He weighed 122½ pounds (55.7 Kg). Temperature 101.2° F (38.5° C). Pulse 108. Blood pressure 174/104. The thyroid was enlarged and there was an adenoma in the right lobe, measuring approximately 5x4 cm. The chest and lungs revealed no positive findings. There was no percussible enlargement of the heart. The rate was increased and there were occasional extrasystoles, but no murmurs. Palpation of the abdomen revealed no masses or palpable organs. Neurologic examination showed no abnormalities. There was a rather pronounced digital tremor.

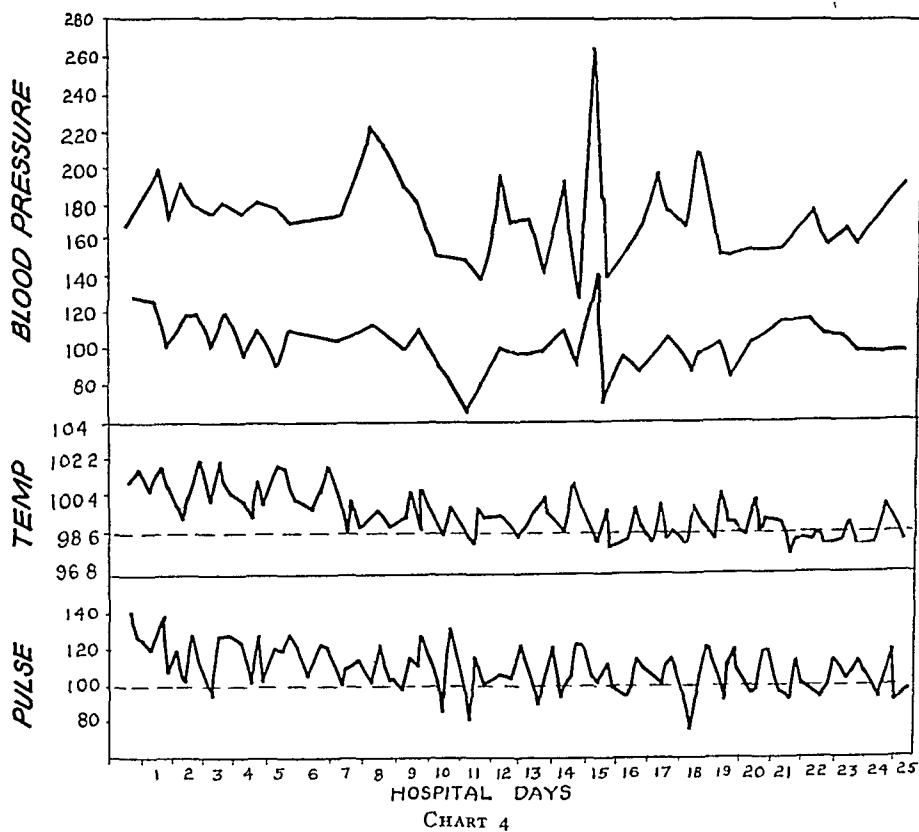
Laboratory Data—Urinalysis showed the pH of the urine to be 7.0, the specific gravity 1.014, with a trace of albumin and 4+ sugar. The urine was microscopically negative for blood. The blood sugar was 405 mg per cent 5½ hours p.c., and the fasting level was 246 mg per cent. The blood urea was 33 mg. The blood count revealed 4,990,000 R.B.C., 14,000 W.B.C., and 86 per cent hemoglobin. Wassermann and Kahn tests were negative. The basal metabolic rate was 36 per cent above normal. The urea clearance was 160 per cent the first hour, and the second hour, 160 per cent. A roentgenogram of the chest, November 8, 1937, was normal. *Clinical Diagnosis*—Nodular goiter, with hyperthyroidism, essential hypertension, diabetes mellitus.

The patient was admitted to the hospital for preoperative preparation for thyroidectomy, during which time his diabetes was cared for, and a search made for the cause of the low-grade fever. Undulant fever agglutination was negative. A furuncle developed on the left forearm which required incision and drainage, others appeared later and when these disappeared, the temperature returned to normal.

A record of the blood pressure in the hospital is shown in Chart 4. It is interesting to observe that abnormally high readings were recorded on two occasions, the highest being 270/150. All readings, however, were at hypertensive levels.

The other significant observation made during his preoperative sojourn in the hospital was a pronounced polyuria. The urinary output varied from 9,000 to 16,800 cc in 24 hours, this was attributed to an associated diabetes insipidus.

In view of the high basal metabolic rate, it appeared that the ideal treatment of the diabetes would include a relatively high calorie diet. His diet contained carbohydrates, 280 Gm, protein, 86 Gm, and fat, 100 Gm, supplying 2,364 calories daily. Amorphous insulin was given in four doses daily, the total daily dose varying between 50 and 150



units and was altered according to uranalysis done on four specimens daily and on blood sugar determinations done as often as three or four times daily. Chart 5 shows the extreme variation in blood sugar levels.

After 26 days in the hospital, his condition appeared not to have changed greatly, but he seemed to have reached maximum improvement and a subtotal thyroidectomy was performed. Although he had a rather sharp postoperative reaction this had subsided by the fourth postoperative day, and a normal convalescence was anticipated. However, on that day a furuncle appeared on the left cheek, which was quickly followed by cellulitis. In spite of all supportive measures the patient went rapidly downhill and died the following day.

Autopsy—Only the pertinent findings at autopsy need be included for our purposes. Upon examining the abdomen the left kidney was in the normal position and of normal size. Occupying the right kidney region was a large, irregular, smooth, somewhat cystic mass the size of a grapefruit, which apparently involved the upper pole of the right kidney. The lower pole of the right kidney was easily felt and was considered to be of normal size and consistency. Lying on the aorta, just below the level of the renal

arteries, was a definitely encapsulated tumor nodule about 1.5 cm in diameter which was similar in gross characteristics to the large tumor in the right suprarenal area.

Later dissection of the large mass showed it to be separable from the kidney and it was then recognized to be a large adrenal tumor (Fig. 2). The entire mass weighed 735 Gm and was about 16 cm in its greatest diameter. It was irregularly spherical and appeared to arise in the medulla of the right adrenal. On section, the tumor had a very large irregular central cavity, the lining of which consisted of a thick, shaggy, necrotic membrane. Surrounding this cavity was a mantle of tumor tissue varying from 2 to 3 cm in thickness. In some areas the tumor appeared grossly to be very cellular, white in color, and to have relatively little stroma. In other areas the tissue was firmer, had a dusky, grayish-brown surface, and was traversed by considerable fibrous stroma. There

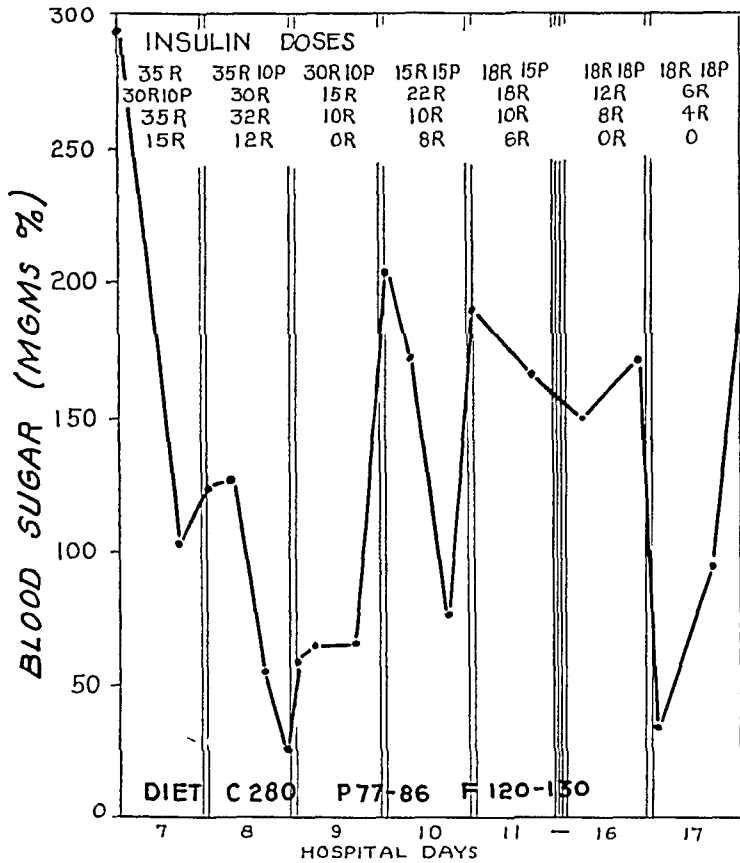


CHART 5

was a fairly thick zone of quite dense sclerotic connective tissues separating the mantle of the tumor tissue from the shaggy lining of the central cavity.

The left adrenal weighed 15 Gm, which is about the normal weight of both adrenals. No tumor nodules were present.

Histologic Examination—Sections from both adrenal glands showed large quantities of cortical tissue, the cells of which were quite large and stained less intensely and uniformly than usual. The cortical zones were not as well defined as usual. There appeared to be less than the usual amount of medullary tissue. Sections of the right adrenal showed an encapsulated tumor composed of cells of a single type but with extreme variations in size, shape and staining reaction. In general, they were comparable to the cells of the medulla rather than of the cortex. A section of the nodule removed from below the level of the renal vein showed the tumor cells to be of a type similar to those of the large tumor. **Pathologic Diagnosis**—Pheochromocytoma of the right adrenal.

An associated finding of interest was the presence of cardiac hypertrophy, the heart weighing 450 Gm. The left ventricular wall averaged 2 to 2.5 cm in thickness, the

right ventricular wall averaged 0.7 cm. There were moderately advanced atheromatous changes present in the aorta. The kidneys were grossly and microscopically normal and showed no active inflammatory process, and little or no sclerosis of blood vessels or glomeruli.

COMMENT —The short duration of symptoms in this case is remarkable. Before operation it was observed that spikes of hypertension occurred but such elevations of blood pressure were thought to be associated with insulin reactions. In retrospect, it appears that we were unable to distinguish the symptoms due to frequent hypoglycemic episodes from a very similar set of symptoms which may have been associated with paroxysms of hypertension due to outpouring of large amounts of epinephrine, the patient's sympathetic nervous system being severely disturbed in both instances.

The blood sugar levels on the same food intake were extremely variable. It is not unusual for an individual with severe diabetes who is having his disease brought under control quickly to have insulin reactions, and, at first, in this case little attention was given to these. However, as days passed it was mentioned more than once at his bedside that it seemed remarkable for his blood sugar levels suddenly to fall to such low range without obvious explanation. Levels of 28 mg per cent, for instance, were found. Later our attention was called to the fact that spells of nervousness, weakness and profuse perspiration occurred, which were considered at the time to be insulin reactions, yet blood sugar levels such as 98 mg per cent, for example, were demonstrated at the height of symptoms. It was assumed that the extreme instability of the blood sugar levels was further exaggerated by hyperthyroidism and active infection. In the light of our present information the explanation would appear to be about as follows. First, it is probably correct to assume that the pressor substance released by such tumors is epinephrine (*vide infra*). When the amount of epinephrine poured out by the tumor was large, the glycogen was freed from the liver at a rapid rate, raising the blood sugar level. So long as this rate of epinephrine production was maintained, large amounts of insulin could be tolerated, but when it was withdrawn the blood was no longer flooded with sugar poured into it from the liver, and the insulin would cause a more rapid than normal deposition of glycogen in the liver, with tissue lack elsewhere and hypoglycemic shock. Whether diabetes actually existed might possibly be questioned, although in view of high fasting blood sugar levels and glycosuria, this seems acceptable. It is evident that the factors here are not present in the same relative proportions as are usually seen. There probably was some inherent weakness in the regulating mechanism for glucose metabolism, however, since other patients with high blood pressures from pheochromocytomata do not necessarily have anything comparable to clinical diabetes mellitus. Perhaps, if a more critical analysis of the oscillating blood sugar levels and of his "reactions" without hypoglycemia had been made, our attention might have been directed toward adrenal disease.

The question may be asked: Did this man have hyperthyroidism? If so was it caused by or was it maintained by excessive quantities of epinephrine?

in the blood? These questions cannot be completely answered. It is noteworthy, however, that he lacked such features of hyperthyroidism as exophthalmos, and presented others such as the extreme redness of the face and tongue as well as marked polyuria and high diastolic pressure not to be explained by thyroid disease. That the rate of blood flow through the tissues was excessive is consistent with his abnormally high urea clearance test, and this is a particularly interesting finding which points to the nonrenal origin of the hypertension. The rapid blood flow itself would be in keeping with the high metabolic rate and may also explain the severe polyuria. There are other points which seem to indicate that the hypermetabolism was of adrenal origin, namely, that his response to iodine was slight or questionable. The thyroid gland was not large, the portion removed at operation weighed 27 Gm. In considering this, it is worth noting that there was thrombosis and hemorrhage present which would increase the weight of the gland. There was a ruptured cyst, however, and some thyroid tissue was found at the lower left pole at autopsy. The pathologic report on the thyroid tissue removed was colloid goiter with a ruptured cyst. This does not offer any evidence that hyperthyroidism existed, and is quite consistent with the assumption that the hypermetabolism was of extrathyroid origin. His blood cholesterol was 125 mg %, which is relatively low, and at a level frequently seen in hyperthyroidism, but this, too, loses its significance in view of the infection present as well as consideration of the relatively low level found in Case 1 in which the hypermetabolism disappeared on removal of the adrenal tumor.

One of the important features of this case was the presence of a secondary tumor lying on the aorta at the level of the renal arteries which had a gross and microscopic appearance identical with those of the large tumor. This probably represents a tumor of the organ of Zuckerkandl. This not only demonstrates the fact that such tumors are sometimes multiple and outside the suprarenal area, but also suggests an explanation for failure to obtain relief in some patients, by the removal of a single growth.

Embryology and Pathology—The adrenal medulla has a common origin with the sympathetic nerve cells arising from the neural crest and is thus ectodermal in origin. It is part of the so-called chromaffin tissue, deriving this name from a brownish discoloration which it undergoes when fixed in a chromate solution. At birth it is represented, in addition to the adrenal medulla, by paraganglionic masses which usually degenerate as the adrenal medulla grows. Such masses may remain, however, and have been recognized chiefly in two locations. Kohn⁵ called attention to a strip of chromaffin tissue situated ventral to the abdominal aorta and superior to the inferior mesenteric artery to which he gave the name paraganglion aorticum abdominale. Zuckerkandl⁶ observed a pair of similar bodies in the region of the inferior mesenteric artery of the newborn, which have been known as the organs of Zuckerkandl. It is quite probable that these are the common sites of origin of aberrant pheochrome tumors, yet it is interesting to observe that in adrenalectomy experiments no hypertrophy or hyperplasia of these tissues

has been observed, which throws some doubt upon their functional capacity. Another chromaffin organ is the carotid body, but so far as we are able to determine, tumors of this organ have never produced sympathetic stimulation, nor have they been associated with hypertension.

Tumors of the adrenal medulla may be of three types: (1) Sympathoblastomata arising from immature sympathoblasts, (2) ganglioneuromata from mature ganglion cells, and (3) pheochromocytomata, from mature chromaffin cells or pheochromoblasts. These have frequently been termed paragangliomata.

We are interested here only in the latter group which are well encapsulated, benign, nonmetastasizing tumors. They do not disturb their host by invasion, but by their functional activity are physiologically malignant. They vary greatly in size, having been observed varying from the size of a pea to that of a grapefruit. The size does not determine their activity. It is quite common for the larger ones to break down centrally, forming necrotic, cyst-like cavities.

They occur about equally in the sexes and although the autopsy cases reported earlier were more common in older people, clinical recognition has been much more frequent in young adults, the average age in the cases reviewed by Howard and Barker⁷ being 27.5 years for the women, and 32 for the men.

There are certain features about these tumors which are of practical interest. For no known reason they are more prevalent on the right side. In the 103 cases reported by Brunschwig and Humphreys¹ there were 43 on the right and 34 on the left, while in the 20 surgical cases tabulated by McKenzie and MacEachern,² 15 were on the right and five on the left, a three to one ratio. In the cases collected by Howard and Barker,⁷ this is even more outspoken, for of the 13 cases in which the tumor was situated in the adrenal gland, ten were on the right and only three on the left. As in our case, others have reported such tumors occurring away from the adrenal or in aberrant or heterotopic adrenals. Phillips⁸ reports a case occurring in the apex of the left pleural cavity. He was able to find in the literature only 11 cases occurring outside the adrenal, and in nine of these the organ of Zuckerkandl was the site of origin, while one of the remaining two cases was in the right pleural cavity. The vast majority, however, will be found by a careful exploration of the renal area.

Microscopically, the tumor consists of nests or cords of polyhedral cells separated by thin connective tissue stroma, rich in capillaries. The cells vary in size and have large nuclei containing chromatin network. Mitoses are rare. Sections of the tumor fixed in bichromate solution show brown pigmented granules or diffuse brown pigmentation present in many, although not all, of the cells. This is evidence of secretory activity and is caused by some strong reducing substance, presumably epinephrine.⁹ Epinephrine has been found to occur qualitatively in these tumors and quantitative determinations have been made, as in the case of Kelly, Piper, Wilder and Walters¹⁰ which

showed 120 mg of crystalline epinephrine in half the tumor, and it was estimated that there would be 300 mg in the entire tumor. All cases in which quantitative determinations have been made in these tumors have shown amounts of epinephrine far in excess of the amount normal for the adrenal medulla.

Diagnosis—The diagnosis in these cases may be made by a careful analysis of the history. Paroxysmal attacks of hypertension have been recorded as the outstanding symptom in most cases, and this may be associated with precordial pain, tachycardia, pallor and flushing, and sensation of cold followed by heat, sweating, nausea and vomiting are not uncommon. Paroxysmal hypertension is not a prerequisite for the diagnosis, the hypertension being constant during the last period of observation in our first case. Persistent hypertension associated with pheochromocytomata has been mentioned previously by Wells,¹¹ and emphasized by Edward.¹² Vasomotor disturbances of some type which usually appear in definite seizures, apparently are present in all cases. Certain cases have simulated hyperthyroidism so closely as to lead to thyroidectomy. An elevated basal metabolic rate was present in both of our cases. This has also been reported by others.^{2, 7} In seven of the cases in which the basal metabolic rate was recorded it was found to be distinctly elevated in three. In certain instances massage over the tumor may result in a sharp rise in the blood pressure.

We have been impressed with the unusually high renal function observed in our two cases. It appears that the secretion of these tumors stimulates the normal kidneys to increased function. In some cases diminished renal function may result from the disease. Also, as the result of the increased epinephrine, glycosuria and hyperglycemia are commonly observed.

There are several methods by which the roentgenogram may be of assistance in reaching a diagnosis. Often the plain film reveals a tumor shadow in the suprarenal area. Indirect evidence is also obtained by doing an intravenous urogram or a bilateral pyelogram, to see if there is any downward displacement of either kidney. Howard and Barker⁷ stated that 11 of their 18 cases would have been demonstrated by making a pyelogram. A pyelogram in our second case would obviously have demonstrated the presence of a mass, but no change was observed by pyelography in our first case. In pyelography the size of the tumor is the important factor, and a tumor of considerable size is required to displace the kidney. Earlier methods of diagnosis of value before tumors reach such a size are desirable.

Visualization of these tumors by perineal air injection has been employed by many, and its use in visualizing these tumors has been acknowledged by all. It is, however, not without risk, and fatalities have been reported from its use. Cahill¹⁴ recently reported a large series of air injections, and feels that it is quite safe if certain fundamental precautions are observed. Joelson¹⁵ has employed the procedure in a considerable number of cases without a serious event and feels that the secret of safety lies in the slowness of injection of the air. He takes 40 to 45 minutes to inject 300 to 400 cc, and in this manner

avoids all unpleasant sensations for the patient. We have done a small number of an injections and, although no fatalities have occurred, there have been two patients with reactions severe enough to cause hesitation in advising the procedure unless clear-cut indications are present. In cases in which a tumor is strongly suspected but cannot be demonstrated, we believe the surgeon should be prepared to undertake a bilateral exploration.

Treatment—The treatment is surgical removal of the tumor, which can be expected to result in a cure, for this has been the result in all reported cases successfully operated upon, some now many years since operation. Even in the patients with persistent hypertension, removal of the tumor resulted in a prompt return of the blood pressure to normal.

The choice of operation depends upon a number of factors, not the least of which is individual preference. We have preferred the retroperitoneal operation after the technic described by Young,⁴ which permits simultaneous bilateral exposure of the adrenals and avoids the increased risk of the transperitoneal approach. In cases in which the tumor is large, resection of the twelfth rib would greatly facilitate the operation.

The predilection of the tumors for the right side is worth remembering, but if there has been any doubt as to the side the tumor is on, this may be dispelled at the operating table, as in our case, even before the tumor is exposed. Manipulation of the area will produce a sharp rise in both the systolic and diastolic blood pressures, and when exposed, even the lightest pressure on the tumor is reflected in the blood pressure. The event, however, which requires careful preoperative planning is the clamping of the vessels and removal of the tumor. This is generally followed by a profound fall in blood pressure and possibly a state of shock. An ample supply of epinephrine must be ready, and in our case repeated doses were necessary in order to maintain the blood pressure. In addition to this, transfusion is almost essential, and this should be administered both during and after operation until the blood pressure is stabilized. We employed plasma transfusion during operation in our case, which served admirably to support the circulation.

Spinal anesthesia should be avoided because of its tendency to reduce the blood pressure. Basal anesthesia with avertin supported by light nitrous oxide and oxygen was satisfactory in our case.

No other method of treatment has been of any benefit. Deep roentgenotherapy has failed to bring any relief in the cases in which it has been tried. Nor is there any satisfactory palliative treatment for the attacks. Amyl nitrite has been suggested to relieve the hypertensive seizures in those patients presenting paroxysmal hypertension, but the nitrites otherwise have been of little benefit.

The recognition of the disease is most important, so that one may advise against any other operation, for these patients are poor operative risks and some of the deaths in such cases have followed other operations. Therefore, the only operation which should be performed is for the removal of the lesion which is producing the disease.

SUMMARY

Two cases of pheochromocytoma of the adrenal gland are presented

In one case, severe diabetes mellitus existed, together with an extreme polyuria, amounting to as much as 16,800 cc per day

One of the cases was correctly diagnosed preoperatively with the help of clinical data and without the aid of demonstration of a tumor. In this case operative removal of the tumor has led to a complete cure

It has been emphasized that paroxysms of hypertension are not a necessary part of the syndrome accompanying these tumors. The presence of hypermetabolism has been an outstanding feature in these cases. It is probable that hyperthyroidism was not present in either case and, in one, the hypermetabolism disappeared following removal of the tumor. Attention has been called to the diagnostic importance of high urea clearance

REFERENCES

- ¹ Brunschwig, A, and Humphreys, E. Excision of Pheochromocytoma Following Near Fatal Attack of Paroxysmal Hypertension. *J A M A*, **115**, 355-357, August 3, 1940
- ² McKenzie, D W, and MacEachern, D. Tumor of Medulla of Adrenal (Adrenal Pheochromocytoma) with Removal and Relief of Paroxysmal Hypertension. *Jour Urol*, **40**, 467-476, October, 1938
- ³ McCullagh, D R, and McLin, T R. Extraction of Androgens from Urine. *Endocrinol*, **22**, 120-121, January, 1938
- ⁴ Young, H H. Technique for Simultaneous Exposure and Operation upon the Adrenals. *Surg, Gynec, and Obstet*, **63**, 179-188, August, 1936
- ⁵ Kohn, A. Das chromaffine Gewebe. *Ergeb Anat und Entwicklungsges*, **12**, 235, 1902
- ⁶ Zuckerkindl, E. Nebenorgane des Sympathicus im Retroperitonealraum des Menschen. *Anat Anz Ergänzungsheft*, **19**, 95, 1901
- ⁷ Howard, J E, and Barker, W H. Paroxysmal Hypertension and Other Clinical Manifestations Associated with Benign Chromaffin Cell Tumors (Pheochromocytoma). *Bull Johns Hopkins Hosp*, **61**, 371-410, December, 1937
- ⁸ Phillips, B. Intrathoracic Pheochromocytoma. *Arch Path*, **30**, 916-921, October, 1940
- ⁹ Beer, E, King, F H, and Prinzmetal, M. Pheochromocytoma with Demonstration of Pressor (Adrenalin) Substance in the Blood Preoperatively during Hypertensive Crises. *ANNALS OF SURGERY*, **106**, 85-91, July, 1937
- ¹⁰ Kelly, H M, Piper, M C, Wilder, R M, and Walters, W. Case of Paroxysmal Hypertension with Paraganglioma of Right Suprarenal Gland. *Proc Staff Meet, Mayo Clinic*, **11**, 65-70, January 29, 1936
- ¹¹ Wells, A H, and Boman, P G. Clinical and Pathological Identity of Pheochromocytoma. *J A M A*, **109**, 1176-1180, October 9, 1937
- ¹² Edward, D G F. Pheochromocytomata and Hypertension. Details of Case. *Jour Path and Bact*, **45**, 391-403, September, 1937
- ¹³ Binger, M W, and Craig, W M. An Atypical Case of Hypertension, with a Tumor of the Adrenal Gland. *Proc Staff Meet, Mayo Clinic*, **13**, 17-20, January 12, 1938
- ¹⁴ Cahill, G F. Air Injection to Demonstrate the Adrenals by X-ray. *Jour Urol*, **34**, 238-243, September, 1935
- ¹⁵ Joelson, J J. Personal communication

SACROCOCCYGEAL TERATOID TUMOR

CASE REPORT

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THE COMPLEX TERATOID TUMORS of spectacular appearance are rare neoplasms. They occasionally present difficult diagnostic and therapeutic problems. The sites of occurrence in the order of their frequency are the pelvis, the abdomen, the sacrococcygeal region, the thorax, and infrequently the nervous system. The teratomata of the newborn usually have a disorderly arrangement of germ layers, described by Ewing as a "pot-pourri" of fetal tissues. The presence of derivatives from all three germ layers, in contradistinction to the dermoid tumor, which is of ectodermal origin only, classifies these tumors as teratomata. Some teratomata may exhibit a more adult structure of their germ layers, even approaching the parasitic fetus, in whose development there is a more or less normal arrangement of organs. To this group, Ewing has applied the term "teratoid tumors."

A great variety of organs in various stages of development have been found, *e g*, from the ectoderm—nerves, epidermis and dermoid cysts, from the entoderm—bronchus, intestine, pancreas, liver and adrenal gland, and from the mesoderm—fibrous tissue, cartilage, bone, smooth and striated muscle. The sacrococcygeal teratoid tumors seem to be more prolific in producing rudimentary organs than those arising in other sites. The bone tissue may actually condense into well-formed extremities such as a forearm, hand, tibia, femur or toes. It requires no imagination to conceive of these complex sacrococcygeal tumors as the abortive half of a fused, monstrous, pygopus twinning.

The teratoid tumor, with its great degree of tissue differentiation, seldom undergoes cancerous transformation. It has been asserted that the benignity of such a tumor can be assured, if muscle twitching, peristalsis or the presence of bone can be demonstrated. This statement is practically true, but there have been isolated examples of embryonal cancer developing in these tumors with local recurrences after removal and distant metastases causing death (De Vee, Bowdler, Renner, Goodsitt, Stewart and Craig).

Diagnosis—In the group of published case reports, these tumors are more common in females than males—a ratio of more than 3 to 1. The presence of the tumor is usually observed at birth—65 of 72 cases, as reviewed by Chaffin. The tumor may be sufficiently bulky to complicate the delivery of the infant. If situated intrapelvically, the diagnosis may not be suspected until urinary or bowel destruction occurs.

The sacrococcygeal teratoid tumor must be differentiated from a pilonidal cyst, meningocele, dermoid cyst and congenital anal atresia. A careful physical examination, and roentgenologic studies, usually lead to the correct

diagnosis The meningocele is compressible, and such pressure will cause bulging of the anterior fontanelle, furthermore, coughing and crying produce an expansile pulsation which is lacking in the teratoid tumor. The discovery of extraskletal bone in the roentgenograms establishes the diagnosis of teratoid tumor. Although neurologic changes are not often associated with sacrococcygeal teratoid tumors, it should be borne in mind that defects of the spinal column, spinal cord and membranes may occur.

All sacrococcygeal teratoid tumors originate retroectally, although they may arise dorsal or ventral to the sacrum. The teratomata situated on the dorsal aspect of the sacrum (see present case report) are rare in comparison with the same tumors springing from the anterior aspect of hollow of the sacrum. The origin is usually between the rectum and lower segments of the vertebral column, the tumor often grows downward to become extruded and hang as a sessile or pedunculated mass between the legs. If the tumor remains within the pelvis, obstruction to the urethra and rectum may occur.

Treatment—Ewing has stated that one-third of the fetuses with sacrococcygeal teratoma are born dead and 90 per cent of the others die soon after birth. Those infants who survive should have their tumors removed as soon as their physical condition permits. The deformity itself sufficiently justifies the operation. Even though the tumor presents posteriorly, its growth may result in destruction, by pressure, of the gluteal muscles and fat. Pressure necrosis, ulceration and secondary infection in the tumor itself are serious complications of delay in treatment. The surgeon must use great judgment in deciding the optimal time for excision. The shock associated with this operation may be greater than expected. The intrapelvic teratoid tumors present a more difficult surgical problem. Inasmuch as these tumors are extraperitoneal and arise posterior to the rectum, the approach should never be through a suprapubic incision, but rather by resecting the coccyx and, if necessary, the terminal vertebrae (Peaise). In some instances the tumor can be shelled out without sacrificing any of the lower vertebral column, but the surgeon should never hesitate to do so to assure adequate exposure and complete removal.

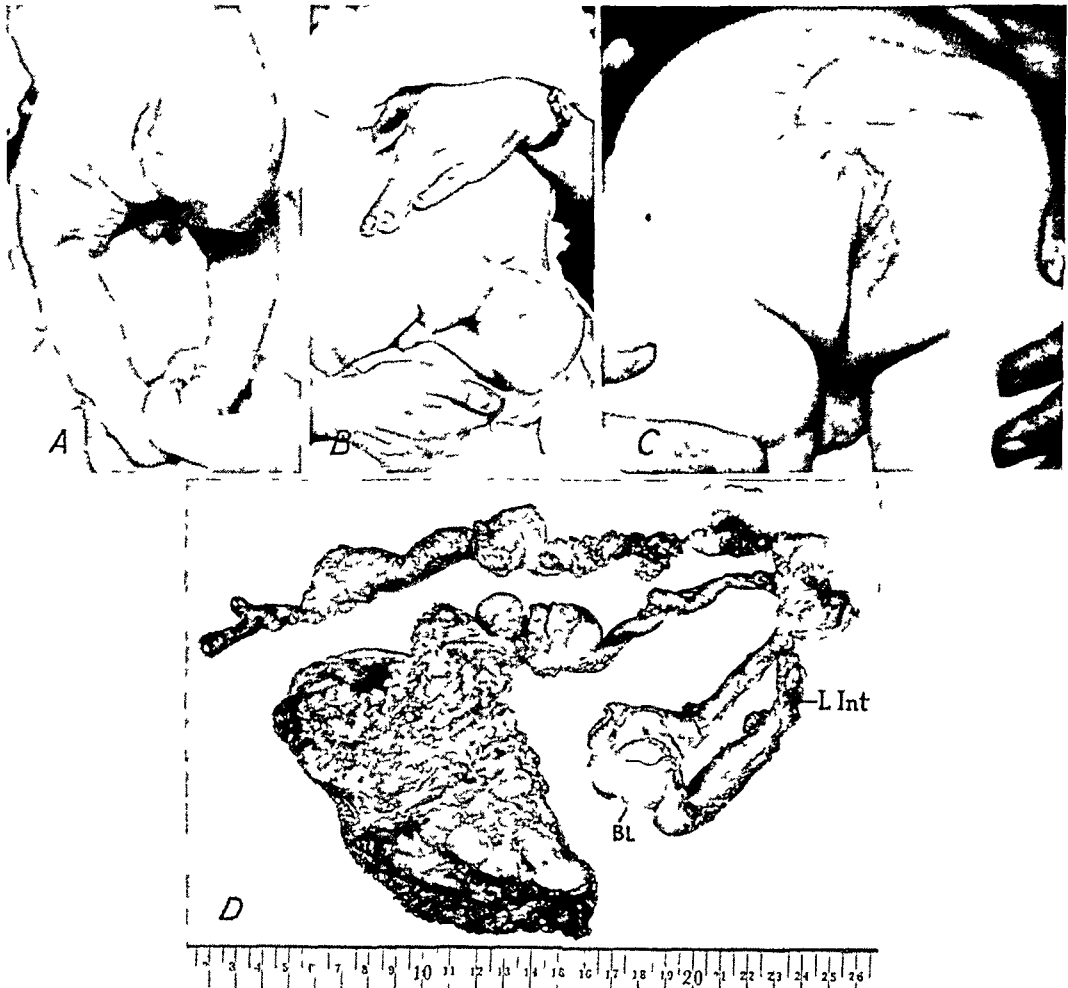
Case Report—A. B., a male infant, four weeks old, was admitted to the Mixed Tumor Service of the Memorial Hospital, April 12, 1938. The delivery was reported as being normal, spontaneous and full-term. Since birth, the infant had been a feeding problem, and the third successive formula was being tried. A definite maternal and paternal history of twinning was obtained.

History—At birth, a tumor mass was observed over the lower spine and right buttock. This increased in size in proportion to the child's growth. The mother stated that at birth there was a small but definite rudimentary umbilical cord attached to the mass. This later sloughed, leaving a small ulcer which remained unhealed. The mother also noted that when the child nursed there was a contraction over the lower portion of the mass. The tumor apparently caused the infant no pain and little inconvenience.

Physical Examination—The child was a well-developed, slightly undernourished male infant, with a prominent tumor mass, measuring 8x7x4 cm., overlying the lower sacrum and right buttock. The tumor was covered by intact, elastic skin, except at one edge where there was a puckering of the skin which suggested a rudimentary umbilicus. The presence of this navel and antecedent cord indicated a high degree of tissue differen-

tration, approaching a parasitic fetus in character. The consistency of the mass varied, in the upper portion were several small, round fluctuant lobules, in the lower portion an irregular, firm nodule with definite skin attachment, resembling cartilage or bone. Stroking of the overlying skin produced two types of motility: (1) A superficial contraction of the skin, not unlike that seen in the cremasteric reflex, and (2) a deep vermicular movement similar to peristalsis within the contents of the mass. The child

PLATE I



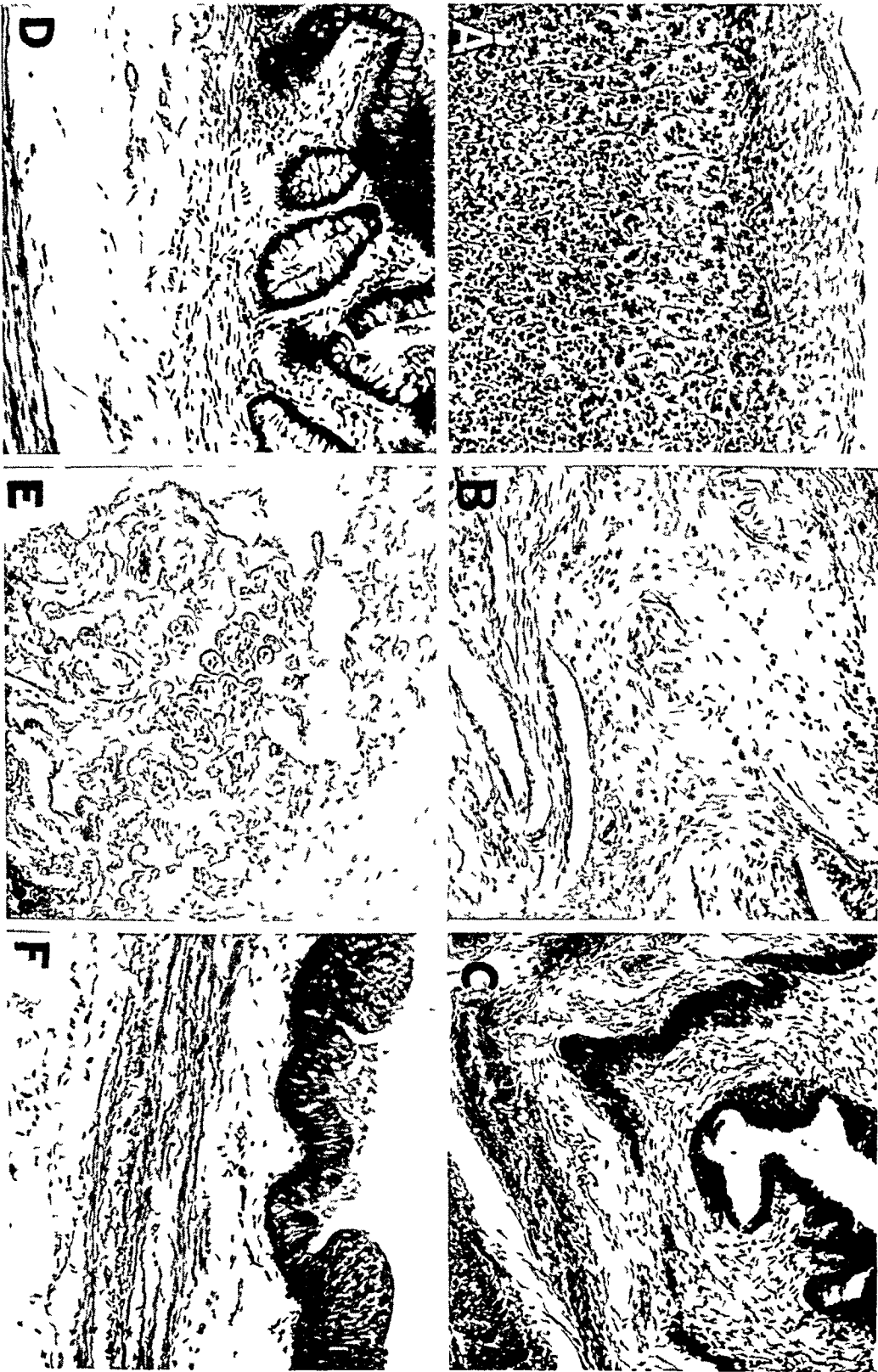
- (A) Infant age six weeks sacrococcygeal teratoid tumor
 (B) Same infant age 13 months Preoperative condition
 (C) Postoperative condition
 (D) Gross specimen, showing 78 cm of intestine, Bl = urinary bladder, L Int = large intestine

was permitted to nurse and, on swallowing, the same contractions took place as were produced by stroking. No sensory or motor changes could be demonstrated in the lower extremities. There was pronounced dilatation of the superficial abdominal veins. Roentgenologic studies showed no apparent defect in the sacrum and coccyx. Bony shadows of different densities were visualized roentgenographically within the tumor.

Treatment—Surgical removal was not considered advisable until a later date because of the age, poor state of nutrition, and general physical condition of the child. Periodic examinations were made until the child was one year of age, at which time it was admitted for surgical excision of the tumor. During this year of observation, the increase in size of the tumor was not disproportionate to the growth of the child, as a whole.

Operation—Performed under ether anesthesia, April 5, 1939. The tumor was excised

PLATE II



(A) Well formed adrenal gland
(B) Brain
(C) Urinary bladder
(D) The medulla is lacking
(E) Large intestine
(F) Bone and cartilage
(F) Bronchus

through a wide elliptical incision. The dissection was relatively close to the capsule of the tumor and a good plane of cleavage was encountered except at the base where there was a stalk-like attachment to the sacrum. Adequate skin flaps permitted closure of the wound with interrupted silk sutures. A marginal stab wound was made for drainage. The postoperative course was uneventful, apart from a slight wound infection near the anus. The patient was discharged in good health on the seventeenth postoperative day. The child was seen recently (October, 1941) and showed no evidence of residual tumor. There was only a slight central depression of the scar over the sacrum.

Pathologic Examination—The specimen consisted of an excised mass, surmounted by an ellipse of skin, measuring 8x10 cm. The subcutaneous tumor was made up of fat, connective tissue, bone, fragments of hair and a large length of intestine, which, when uncoiled, measured 78 cm in length. It was divided into segments by occlusion of the lumen and contained a thick, greenish, mucoid substance which was chemically negative for the presence of bile. Along the course of this loop of intestine were situated three small out-pocketings, which contained clear, thick, mucoid material. A fourth globular out-pocket contained clear, watery fluid. *Microscopically*, this cloacal sac, or *diverticulum*, was identified as urinary bladder. *Microscopic study of various parts of the tumor* disclosed structures identifiable as well-formed adrenal (lacking medulla), poorly formed brain, fetal fat, epidermis, well-formed urinary bladder, large intestine, bone cartilage, and questionable bronchus.

REFERENCES

- ¹ Brines, R. J. A Large Teratoma Containing Rudimentary Arm Bones and a Hand. *J A M A*, 103, 338, 1934.
- ² Bucy, P. C., and Buchanan, D. N. Teratoma of the Spinal Cord. *Surg, Gynec, and Obstet*, 60, 1137, 1935.
- ³ Bucy, P. C., and Haymond, H. E. Lumbosacral Teratoma Associated with Spina Bifida Occulta. *Am Jour Path*, 8, 339, 1932.
- ⁴ Buddle, M. Cited by Rosedale.¹⁶
- ⁵ Chaffin, L. Clinical Aspects of Sacrococcygeal Teratomas. *Surg, Gynec, and Obstet*, 69, 337, 1939.
- ⁶ Ewing, J. Neoplastic Diseases. Philadelphia, W. B. Saunders Company, 1928.
- ⁷ Hansmann, G. H., and Berne, C. J. Sacrococcygeal Teratoma. *Arch Surg*, 25, 1090, 1932.
- ⁸ Harrington. Cited by Love and Molrsch.¹⁰
- ⁹ Hundling, H. W. Ventral Tumors of the Sacrum. *Surg, Gynec, and Obstet*, 38, 518, 1924.
- ¹⁰ Love, J. G., and Molrsch, F. P. Sacrococcygeal Teratoma in the Adult. Report of a Case. *Arch Surg*, 37, 949, 1938.
- ¹¹ McKnight, H. A. Sacrococcygeal Teratoma in Newborn. *Am Jour Surg*, 46, 387, 1939.
- ¹² Middeldorpf. Cited by Love and Molrsch.¹⁰
- ¹³ Morris, K. A. Sacrococcygeal Teratoma. Report of a Case. *Am Jour Surg*, 33, 285, 1936.
- ¹⁴ Pearse, H. Removal of Ventral Tumors of the Sacrum by the Posterior Route. *Surg, Gynec, and Obstet*, 33, 164, 1921.
- ¹⁵ Renner, R. R., and Goodsitt, E. Sacrococcygeal Teratoma. Report of a Case of Double Tumor in New-born Infant. *Am Jour Cancer*, 24, 617, 1935.
- ¹⁶ Rosedale, R. S. Sacrococcygeal Teratoma. Report of a Case. *Am Jour Path*, 11, 323, 1935.
- ¹⁷ Stewart, J. D., Alter, N. M., and Craig, J. D. Sacrococcygeal Teratomata with Malignant Degeneration in Childhood. *Surg, Gynec, and Obstet*, 50, 85, 1930.
- ¹⁸ deVeer, J. A., and Browder, J. Sacrococcygeal Teratoma. *ANNALS OF SURGERY*, 105, 408, 1937.

MALIGNANT DEGENERATION OF NEUROFIBROMATA OF PERIPHERAL NERVE TRUNKS (VON RECKLINGHAUSEN'S DISEASE)*

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THE MALIGNANT DEGENERATION or metaplasia of neurofibromata of the large nerve trunks in von Recklinghausen's disease is the object of this report. Hosoi tabulated 65 cases in 1931, and since then several reports have appeared in the literature. The benign forms of the disease are often overlooked by the surgeon, but not by the dermatologist, whereas the dangers of incomplete operations or irritation of these tumors in peripheral nerves are almost unappreciated by surgeons, although pathologists, such as Ewing, have called attention to them.

Peripheral nerves composed of bundles of neuraxones running out from central nerve cells are bound together by various sheaths for the nerve trunk. Each neuraxone is surrounded by a sheath, the endoneurium is the connective tissue sheath outside the sheath of Schwann which encloses myelinated nerves. This endoneurium blends with the perineurium which binds bundles of smaller fibers together to form a fascicle, while the epineurium is a membrane enclosing the entire nerve trunk, composed of mixed collagenous and reticulin fibers. It is probable that peripheral neurogenous tumors, in most cases, develop from these sheaths. Some nerve trunks are even more complex, including sympathetic fibers and ganglion cells which may complicate tumor formation within them.

Ewing has classified the fibrous tumors arising from nerve trunks as

- (1) Cutaneous neurofibroma (fibroma molluscum, von Recklinghausen's disease)
- (2) Neurofibroma of subcutaneous and deeper nerve trunks, divided into
 - (a) Plexiform neurofibroma
 - (b) Visceral neurofibroma
 - (c) Neurofibrosarcoma (neurogenic sarcoma)

von Recklinghausen's neurofibromatosis has protean manifestations. Many of its tumors have no apparent relation to nerve tissue as such, but may simulate multiple forms of lipoma, myxoma, pure fibroma and the multiple foci of sebaceous gland hypertrophy seen in Pingle's disease. Multiple forms of keloid fibroma may be confused with and included in the concept of neurofibromatosis.

Gairé, in 1892, described primary sarcoma of nerves not associated with von Recklinghausen's disease, and secondary sarcoma of nerves due to sar-

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comatous degeneration of preexisting neurofibromata, a part of von Recklinghausen's disease. Primary sarcoma of nerves is usually very malignant, with rapid growth and invasion of surrounding tissue, leading to internal metastases without local or regional recurrence. In the secondary form, developing in peripheral nerves of patients subjects of von Recklinghausen's disease, the sarcoma develops in one of the preexisting neurofibromata, possibly following trauma or for no known reason, and begins to enlarge quite rapidly. It is at first enclosed in its fibrous capsule where it may remain for a long time. It early becomes painful and later causes excruciating distress in its invasion of large sensory nerve trunks. If operation is undertaken, usually resulting in incomplete removal of the growth, recurrence follows rapidly, with great pain, local growth and distant metastases much delayed. The occurrence of sarcoma in the neurofibroma of peripheral nerves averages from 8 per cent to 15 per cent according to various authors. Other tumors of von Recklinghausen's disease, not necessarily situated in large nerve trunks, seem to be incited to rapid growth and possible malignant degeneration by such operative interference. It is because of the failure of the surgeon to recognize these points that these two case reports, out of 15 instances of neurofibromatosis (von Recklinghausen's disease) admitted to the Presbyterian Hospital, Chicago, appear worthy of record on account of sarcomatous degeneration of large peripheral nerve trunks.

CASE REPORTS

Case 1—R. F., female, married, age 35, was admitted March 10, 1915, finally discharged March 17, 1916. Death in January, 1917, from metastases in the lungs and brain.

She had carried the manifestations of von Recklinghausen's disease, with many tumors, and cafe-au-lait spots, since childhood. Her complaint was a swelling of the left thigh behind the knee, which had begun in June 1915, causing at first dull and later shooting knife-like pains in the sciatic distribution. She was emaciated. There was a history of a fall on the ice 12 years before, followed by development of this tumor and one near the head of the left peroneus longus origin. Her mother, and all of her seven children, had multiple pigmented moles, one brother and one sister had multiple subcutaneous tumors similar to the patient's. The mass of her left thigh measured 47.5 cm in circumference, compared to 25.5 cm for the right thigh. The left leg was normal except for some edema and interfered with function on account of the size of the tumor. Operation to disarticulate the hip was performed March 16, 1915, by Doctor Phemister. A diagnosis of sarcomatous degeneration of neurofibromata (von Recklinghausen) was made. The histology showed many forms of cells varying from small round to spindle in character along with mitotic figures. No nerve tissue was distinguished.

Case 2—O. P., male, age 23, married, was admitted on several occasions between September 16, 1937 and October 2, 1941. This man was studied over four years as a sufferer from neurofibromatosis, with quite large tumors developing in several peripheral nerves—sciatic, radial and median. The tumor in the right median nerve finally led to amputation of the right arm high up, following a diagnosis of sarcomatous degeneration. He is still alive, February, 1942, with no evidence of metastasis.

Since childhood he had had multiple soft tumors of the skin in various parts of the body, along with multiple spots of brownish pigmentation. The tumors were not painful and they now feel like fatty, discrete protrusions, all sessile and not pedunculated. In 1933, he developed a mass in the right thigh, posterior aspect, which has increased in volume until it has reached the size of a grapefruit. This interfered with sitting and full extension of the leg, and was accompanied by pain in the sciatic distribution. Shortly

after the tumor of the sciatic nerve developed, in 1933, there appeared in the right forearm, on the volar aspect, a similar mass which at first was not painful but led to weakness in the hand, although some motions of the hand and fingers were still possible. The principal interference was confined to median nerve distribution.

The thigh tumor seemed so hard in one area that calcification was suspected, although the tumor seemed to infiltrate into the muscle spaces like a diffuse lipoma. It was evidently part of the von Recklinghausen's disease present.



FIG. 1.—Case 2. Back view in 1937, when a small lumbar tumor was removed for histologic examination. The discolored (café au lait) spots and innumerable tumors are seen.

The blood was normal and the Wassermann test was negative. The forearm tumor had begun to become painful for the last five weeks and, in the last four months, had assumed rapid growth. The subjective sensation in the forearm was one of throbbing, accompanied by prickling up and down the arm and constriction near the center of this mass. Some of this distress was relieved temporarily by aspirin and by extending his arm above his head.

On September 18, 1937, one of the small tumors in his lumbar region was removed for histologic study. This had nonmalignant fibrous characteristics. Two days later, the large tumor of the right thigh and sciatic nerve was removed and showed no malignant findings, nor did there develop any recurrence in the next four years.

On September 28, 1937, a nine-inch incision was made on the volar aspect of the

right forearm. A large whitish mass was uncovered just beneath the bellies of the palmaris longus and the flexor carpi ulnaris, which had been split to expose the field. The tumor was almost cartilaginous in consistency and appearance and was intimately associated with the sheath of the median nerve. Several smaller tumors, more fibrous in character and round in shape, lay in proximity to the main mass. All were dissected away without known injury to the median nerve, though some spots in the sheath of the nerve had to be cut away by the sharp dissection. The nerve was dropped back into place, muscle and fascia were closed over and the skin sutured.



FIG 2



FIG 3

FIG 2—Case 2 Showing tumor of sciatic nerve before removal in 1937
No recurrence to date

FIG 3—Case 2 Forearm specimen (1941) after amputation showing final recurrence after two operations of tumor of median nerve. It is still fairly well encapsulated but the nerve is grossly enlarged in both directions

On section of this mass, no ulceration or destruction of tissue was seen, only loose fibrillar structure in which were embedded spindle- and stellate-shaped nuclei. Most of the fibrils were indistinct with amorphous spaces between them. There were some collections of lymphocytes. No tissue identifiable as nerve fiber could be found.

On August 24, 1940, this tumor had recurred locally, with increased pain, and a second removal was attempted by a similar procedure. At this time, the tissue appeared more collagenous and myxomatous and spread out, invading surrounding tissue and the nerve sheath, extending almost to the elbow, so that complete surgical removal was not possible. A section showed rare mitotic figures. After this wound healed, he was given about 1,000 r roentgenotherapy.

On June 10, 1941, on account of the severe pain, the median nerve just below the elbow was injected first with a small amount of novocain and then with several cubic centimeters of absolute alcohol. At this time, there had now appeared a rapidly growing tumor, nearly the size of a small orange, on the radial nerve at the back of the arm. This was exposed and the mass, 3×1.5 inches, was surgically removed. Its invasion of the nerve was such that the main trunk was severed and, although a few fibrils were preserved, the nerve was mostly destroyed and a drop-wrist followed. A cock-up splint was applied, and for a while the pain disappeared.

Both pain and local recurrence followed rapidly. The tumor again appeared larger in the forearm than it had ever been, and after a clinical diagnosis of sarcoma, amputation of the right arm was proposed and performed, October 3, 1941. The level of the amputation was well above the site of the incision for removal of the tumor on the radial nerve. In the arm tissues it was seen that the middle trunk of the brachial plexus was grossly enlarged and thickened to about three times its normal diameter, as if the tumor mass had invaded this trunk and was extending upward. The cut off trunks of the plexus were injected with absolute alcohol. There had been no local recurrence or metastases yet.

CONCLUSIONS

Development of pain in the distribution of a peripheral nerve, the site of a tumor in a patient afflicted with von Recklinghausen's disease, is highly significant of sarcomatous degeneration of that tumor.

Excision of any tumor mass involving a peripheral nerve in this disease must be cautiously undertaken and thoroughly performed. It may lead to local recurrence and distant metastases or excitation of other tumors of the disease elsewhere in the body.

When sarcomatous change is suspected, early amputation, if possible, is probably the treatment of choice. In the reported cases in the literature, roentgenotherapy in its present state at least seems unavailing.

REFERENCES

- Quick, Douglas, and Cutler, Max. Neurogenic Sarcoma. *ANNALS OF SURGERY*, **86**, 810, 1927.
- Stewart, F. W., and Copeland, M. M. Neurogenic Sarcoma. *Amer Jour Cancer*, **15**, 1235, July, 1931.
- Thompson, Alexis. Neuroma and Neurofibromatosis. Edinburgh, Turnbull and Spears, 1900.
- Jones, Randolph, Jr., and Hart, Deryl. A Discussion of Multiple Neurofibromatosis (von Recklinghausen's Disease). *ANNALS OF SURGERY*, **110**, 916, November, 1939, idem *Trans Am Surg Assn*, **57**, 465, 1939.
- Hosoi, Kiyoshi. Multiple Neurofibromatosis With Special Reference to Malignant Transformation (von Recklinghausen's Disease). *Arch Surg*, **22**, 258, 1931.
- Gentile, Gaetano. Considerazioni clinico-istologiche sopra un caso di morbo di Recklinghausen. *Policlinico (Sez Chir)*, **45**, 407, September, 1938.
- Poursines, V., and Moustardier, G. Evolution sarcomateuse d'une Tumeur Royale de l'Epaule dans une Maladie de Recklinghausen. *Bull Assoc franç p l'étude du cancer*, **27**, 586, June, 1938.
- Ori, J. Leslie. Sarcoma of the Sciatic Nerve and Neurofibromatosis. *Trans Roy Med-Chir Soc Glasgow*, **27-29**, 212, 1932, 1933.
- Trueblood, D. V. Neurogenic Sarcoma. *Surg, Gynec and Obstet*, **72**, No 2A, 363, February, 1941.

CANCER OF THE CERVICAL ESOPHAGUS

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THE ULTIMATE AIM of the surgeon in dealing with diseases of the cervical esophagus has been to devise a safe and adequate operation for the cure of cancer in this locality. A brief review of the history of surgical progress in this field seems indicated, and, although many notable names are identified with this work, it is possible to mention only a few of the major contributions in this report.

The earliest and simplest recorded esophageal operation was an emergency esophagotomy for the extraction of a foreign body carried out by Goursauld,⁸ in 1738. Some 80 years later it was first successfully performed by Roland.¹² Later, in 1833, Ainnott¹ attempted the operation at the Middlesex Hospital, but the patient died 56 hours after operation. In 1858, Cock⁴ had a successful venture, and, in 1868, Cheever¹ reported two successful cases. It is of interest to note a lack of reports in the literature dealing with the surgical extirpation of the cervical esophagus until 1871, when Billroth² reported on his surgical experience with the dogs' esophagus. The paucity of subsequent medical reports dealing with the esophagus in general and the cervical portion in particular leads to the suspicion that a scarcity of suitable operative material, coupled with a shockingly high operative mortality, tended to discourage surgical endeavor along this line.

The cervical esophagus was not considered a suitable province for surgical endeavor until 1877, when the first human cervical esophagus was extirpated by Czerny.⁷ He made an incision along the left anterior border of the sternocleidomastoid muscle, mobilized and excised a segment of cervical esophagus, six centimeters in length, sutured the distal opening into the lower angle of the wound and used it for feeding purposes. His patient made a satisfactory postoperative recovery, but died of recurrent cancer 15 months later. This pioneer operation opened the cervical esophagus to surgical attack.

The second surgical advance in this work was by Mikulicz.¹⁰ In 1884, he resected a cervical esophagus for cancer and performed a plastic-flap repair of the postoperative fistula, which was technically successful and permitted his patient to enjoy eating solid food ten days after operation. Recurrent cancer caused the death of this patient 16 months later.

Von Hacker,¹⁵ in 1908, reported a review of the literature, including a collected series of 25 cases, with an operative mortality of 48 per cent. The longest survival in this group was 16 months. He added a case of his own in which a gastrostomy was followed by a resection of the cervical esophagus and complete extirpation of the larynx. Later, a two-stage plastic procedure was

successful in fashioning a skin tube of two lateral rectangular skin flaps. His patient was living and well 16 months after operation, and had gained 40 pounds in weight, but the final result is not recorded.

Lane,⁹ in 1911, reported that he had resected a cervical esophagus and had

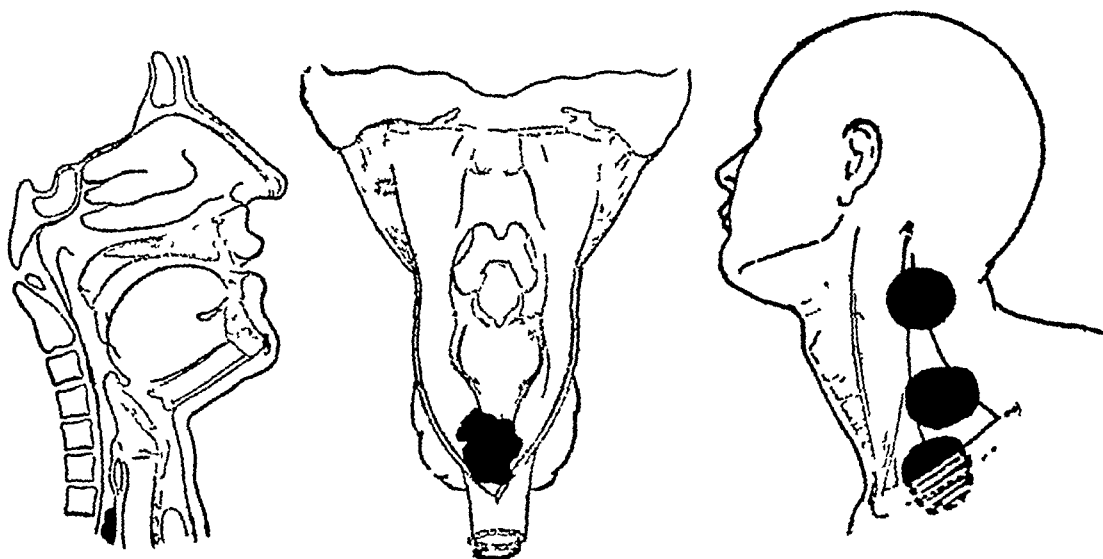


FIG. 1—Case 1. Carcinoma of Upper Esophagus with Cervical Metastases. Treatment: Roentgenotherapy 5 cm port ant neck, 2500 r. Gold filtered radon seeds. Neck nodes—total 103 mc.

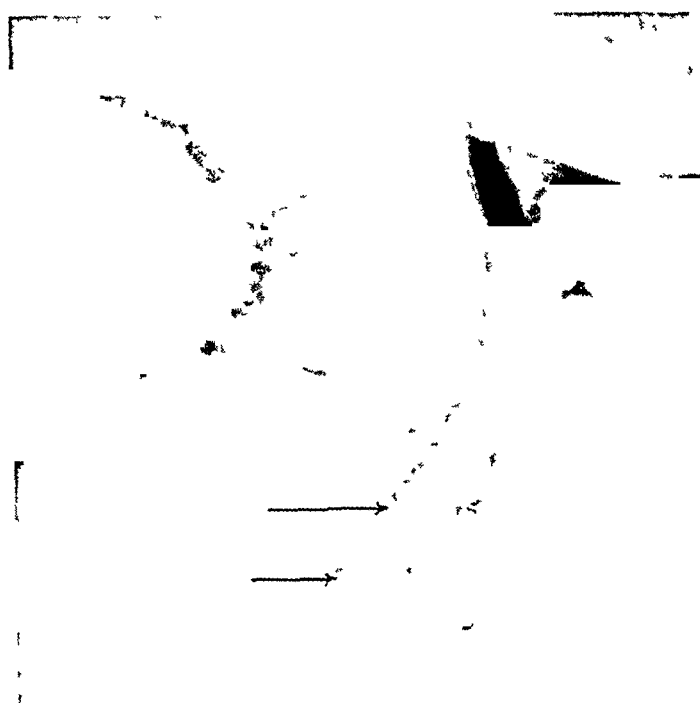


FIG. 2—Case 1. Roentgenogram showing the tumor of the first portion of the cervical esophagus.

used a single horizontal skin flap with its base in the left neck to close the defect, suturing it to the upper and lower edges of pharyngo-esophageal defect. After firm continuity of the tube was established, recurrent cancer invaded the carotid artery and caused a fatal hemorrhage.

Eggers,⁶ in 1925, reported a case of resection of the cervical esophagus and larynx for cancer, and the following year (1926) Torek¹³ reported a similar

case Unfortunately, both these patients died of their disease shortly after operation

Sir Wilfred Trotter,¹⁴ in 1937, reported a ten-year surgical cure His patient came to autopsy and no evidence of cancer was found A considerable amount of hair had grown into the lumen of the reconstructed cervical esophagus

Arthur Evans,⁷ another English surgeon, reported a 23-year cure of cancer of the cervical esophagus by radical excision of the cervical esophagus and larynx

Case 1 reports the successful management by a combination of radiation and surgical measures of a patient with cancer of the cervical esophagus presenting three separate cervical lymph node metastases This patient is alive and in good health five and one-half years later

Case 1—*Carcinoma of Cervical Esophagus* G M, male, age 70, was admitted to Memorial Hospital, April 1, 1936 For a year he had noted the gradual enlargement of a lump in his neck accompanied by increasing nervousness and slight difficulty in swallowing Examination revealed an elderly patient of the thin, wiry, highly nervous type In his left neck, there were three masses The largest one was four centimeters in diameter located beneath the sternocleidomastoid muscle and apparently attached to the left lobe of thyroid gland A smaller mass was noted at a higher level, and the third was partially palpable behind the left sternoclavicular junction (Fig 1)

A node was removed and reported as showing metastatic epidermoid carcinoma, and the working diagnosis of carcinoma of the thyroid had to be dropped Radiographic studies suggested a lesion of the upper cervical esophagus (Fig 2), and direct examination revealed a small outcropping of cancer at the esophageal entrance A biopsy was obtained to confirm the diagnosis

The neck masses were surgically exposed and gold-filtered radon seeds with a value of 88 millicuries were inserted At a later date a dose of 15 millicuries was added, making a total of 103 millicuries Roentgenotherapy was instituted and 2,500 r was administered through a five-centimeter lower neck portal

It is now five and one-half years since treatment was started The patient has gained a little weight, and has no eating difficulties except those he attributes to the lack of a lower dental plate The treated side of his neck is atrophic and fibrotic, with telangiectasis of the overlying skin, and there is a suggestion of a left Horner's syndrome

Five other patients were explored who had cancer of the cervical esophagus and inoperable extensions of the disease found, in each instance gold-filtered radon seeds were inserted at operation, without, however, influencing the rapidly fatal termination of the disease

Jens Nielson,¹¹ of the Radiumhemmet, reported, in 1940, the history of a 48-year-old housewife with cancer of the cervical esophagus free of disease six and one-half years after aggressive radiation therapy The patient was symptom free in 1940, and had gained six kilograms in weight

Case 2—*Carcinoma of Cervical Esophagus* J F, male, age 69, was admitted to Memorial Hospital, July 21, 1937 For three months he had noted gradually increasing dysphagia accompanied by a feeling of substernal pressure and a sore throat

On examination, the patient had the pasty, emaciated appearance, typical of his disease Esophagoscopy revealed a bulky, friable, cauliflower-like mass in the first portion of the cervical esophagus A biopsy study was reported as epidermoid carcinoma,

Grade 2 Roentgenograms revealed a filling defect in the upper esophagus and a soft mass causing partial obstruction of both food and air passageways (Fig 3A and B)

Treatment was by divided doses of roentgen ray, and his reaction was quite severe. The initial edema caused a dangerous narrowing of the trachea and a tracheotomy was necessary. Later, regression of tumor was complete, and the tube was soon discarded. A gain of 17 pounds in weight was noted, and periodic bougie dilatations have maintained a relative freedom from dysphagia for a period of more than four years. Myocardial fibrosis and coronary artery disease complicate this man's prognosis.

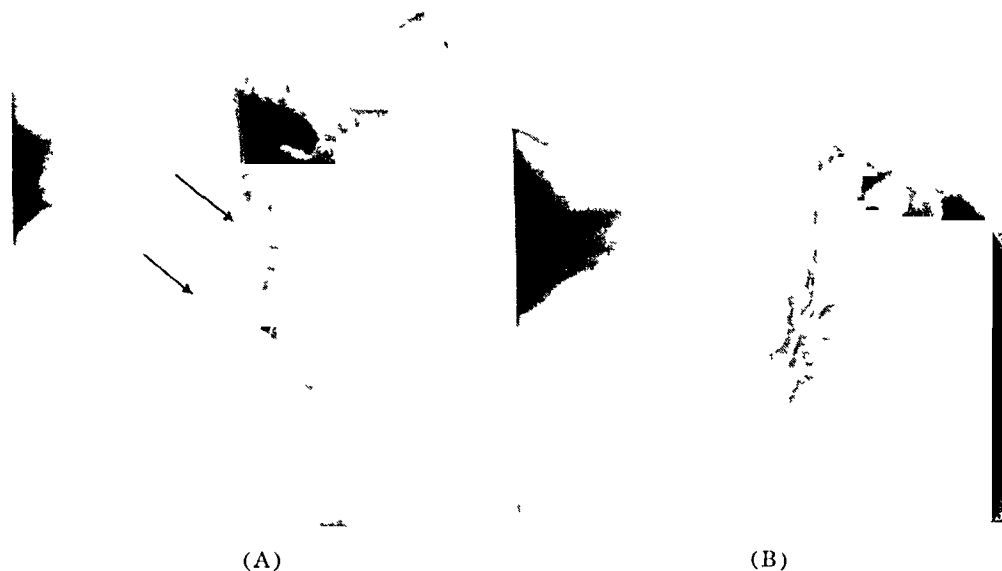


FIG 3—Case 2. Roentgenograms showing (A) the large tumor of the cervical esophagus causing marked tracheal compression and (B) postradiation regression. The patient is alive and well over four years.

It is agreed by most observers that cancer of the cervical esophagus causes one in every 100 deaths due to neoplastic disease. In other words, the disease is a relatively common one, and the material for its study should, therefore, be adequate. Hoarseness, pain and dysphagia are the usual symptoms, and they occur quite early in the course of the disease. The cervical esophagus is well known to be surgically accessible. Given a common disease, located in a readily accessible portion of the body, and calling attention to itself by early symptoms, one may then ask why "cancer of the cervical esophagus is still the realm of experimental surgery."

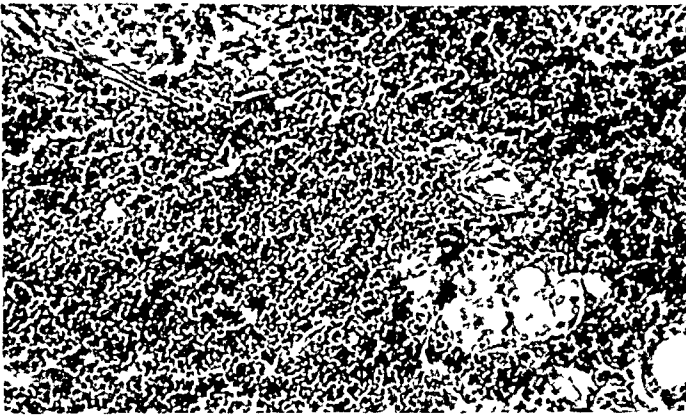
For a number of years, I have been interested in cancer of the esophagus and have reviewed much of the older literature and most of the recent reports dealing with this disease, and it is obvious that there has been a considerable revival of interest in the surgical approach to the problem of cancer of the esophagus. The improved anesthetics now available, the efficient chemicals at hand to combat infection, and an improved surgical knowledge of the parts involved encourage one to take an optimistic position as regards the future control of this disease.

At the same time, it must be remembered that adequate cancer surgery requires not only that the patient make a satisfactory postoperative recovery, but he must also live long enough to warrant the conclusion that his neoplasm has been completely removed. A technically successful operation for the ex-

tirpation of a cancer does not, in itself, entitle the operator to the privilege of reporting his experience

In one recent case of cancer of the cervical esophagus treated by surgical extirpation and plastic repair, the method of attack was suggested by the report of a ten-year cure by Mr. Wilfried Trotter.¹¹ The exact sequence of

(A)



(B)

FIG. 4—Case 3 (A) Cancer of the cervical esophagus (B) Hashimoto's struma

events in our patient's surgical career does not appear in the medical literature of the past, and so may afford a practical basis for future effort and also serve to point out certain pitfalls to be avoided

Case 3—Carcinoma of Cervical Esophagus S. I., female, age 49, had complained of dysphagia for seven years, with occasional episodes of complete obstruction caused by a bolus of food which could be dislodged only by induced vomiting or by swallowing water. A diagnosis of carcinoma of the first portion of the esophagus was established in March, 1940 by Dr. Wm. Wuester, who discovered a small lesion on esophagoscopy and took a biopsy (Fig. 4A). A Janeway-type gastrostomy was performed by him, and the patient was then referred to the Thoracic Surgical Service at Memorial Hospital.

Treatment has been by surgical measures, and a number of steps have been necessary. The first procedure was carried out under intratracheal cyclopropane anesthesia

CANCER OF THE CERVICAL ESOPHAGUS

A wide rectangular incision was made across the lower neck, with its base on the left side. The lower half of the right sternocleidomastoid muscle was excised, revealing a hard, adherent, right lobe of thyroid gland, which was also removed (Fig 5). (Histologically, this proved to be a Hashimoto's struma (Fig 4B) and not cancer infiltration.) The esophagus was mobilized and the prepared skin flap placed behind it and the wound closed (Fig 6). During the subsequent ten days tension and interference with blood

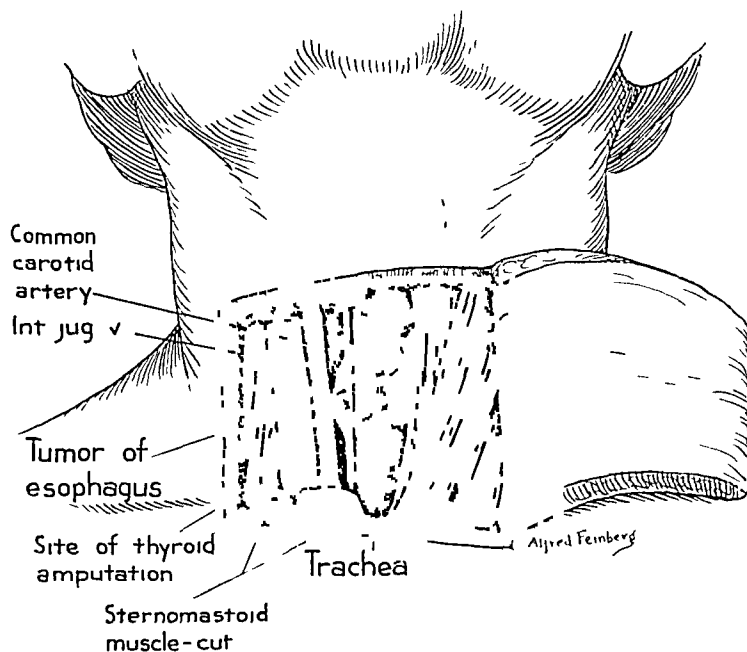


FIG 5—The right sternocleidomastoid and strap muscles have been excised and the right lobe of the thyroid gland removed exposing the cervical esophagus and the tumor.

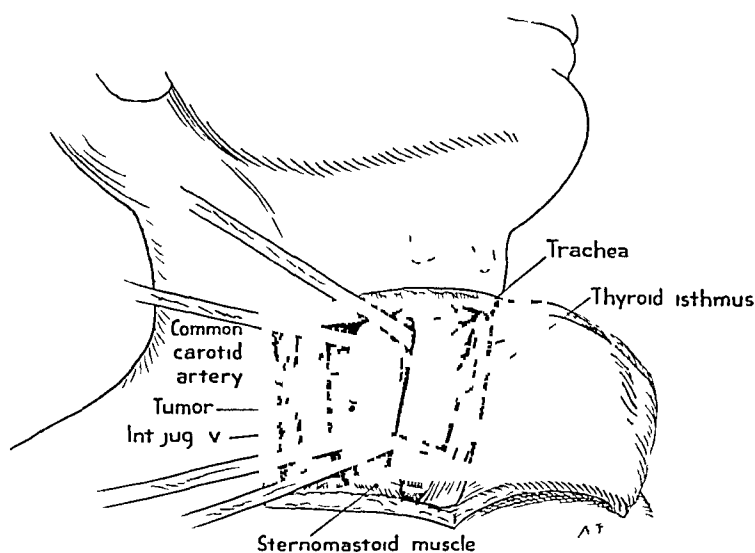


FIG 6—The esophagus has been mobilized and tipes passed around it, above and below the tumor.

supply caused necrosis of the exteriorized portion of esophagus, and at the second operation the necrotic portion was removed by cautery and the upper and lower apertures sutured to the skin (Fig 7).

During the next eight months various unsatisfactory measures were employed in an attempt to maintain a communication between pharynx and esophagus. When the stricture finally closed and obstruction became complete, the first step in the plastic reconstruction was carried out under local anesthesia by opening the right side of neck, excis-

ing old scar, mobilizing trachea and larynx and placing in the defect a large Padgett skin graft. This graft was obtained from a comparatively hairless portion of the right lower abdomen, and it healed in place by primary union (Fig 8)

After an interval of three months, the patient was readmitted and a retrograde esophagoscopy was undertaken and a small olive-tipped bougie was passed upward to

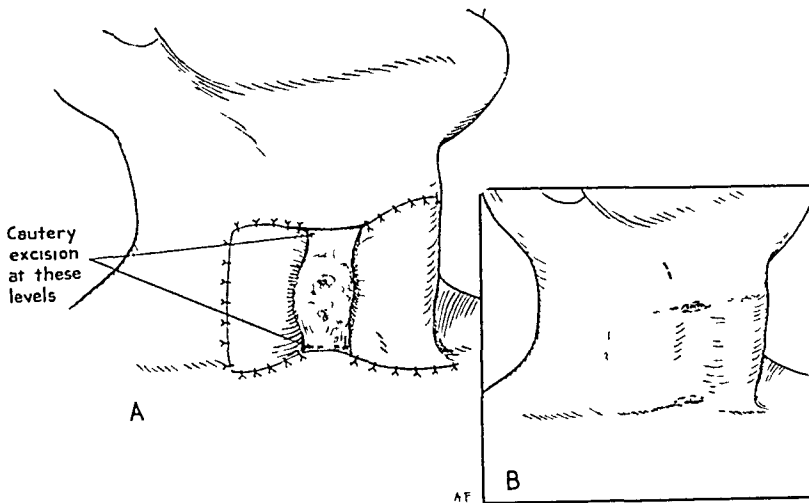


FIG 7—(A) The tumor has been exteriorized by passing the trapezoid flap of skin and platysma beneath the esophagus and closing the incision about it. (B) Ten days later the tumor was excised with the actual cautery.

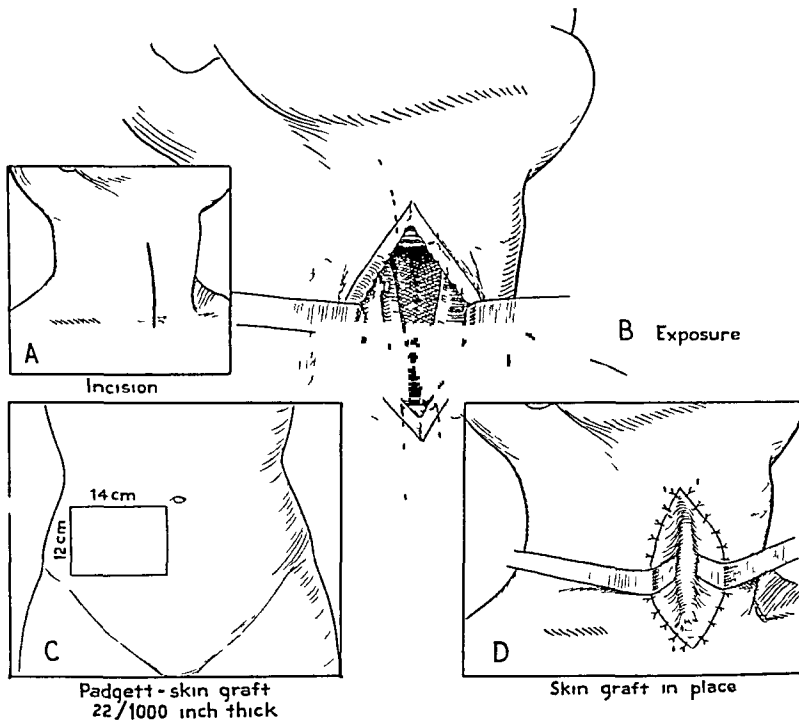


FIG 8—Plastic repair. (A) and (B) show the incision and the exposure. (C) The hairless site of skin graft. (D) The graft in place.

the point of obstruction in the lower neck. A small incision was made in the graft at the point where the bougie could be palpated (Fig 9). A black silk thread was then tied to the bougie and brought out through the gastrostomy stoma. The optimum point for incising into the pharynx was located in the same fashion (Fig 9), and the same black silk thread was then brought out the patient's mouth and anchored to the skin of the cheek (Fig 10).

After a short interval, the apertures were greatly enlarged and an accurate approximation of skin and mucous membrane was obtained

The final operative step was carried out June 3, 1941. The anterior wall of esophagus was formed by infolding the lateral portions of the graft so as to form a continuous tube from pharynx to esophagus (Fig 11). Five grams of sulfathiazole was then placed in the

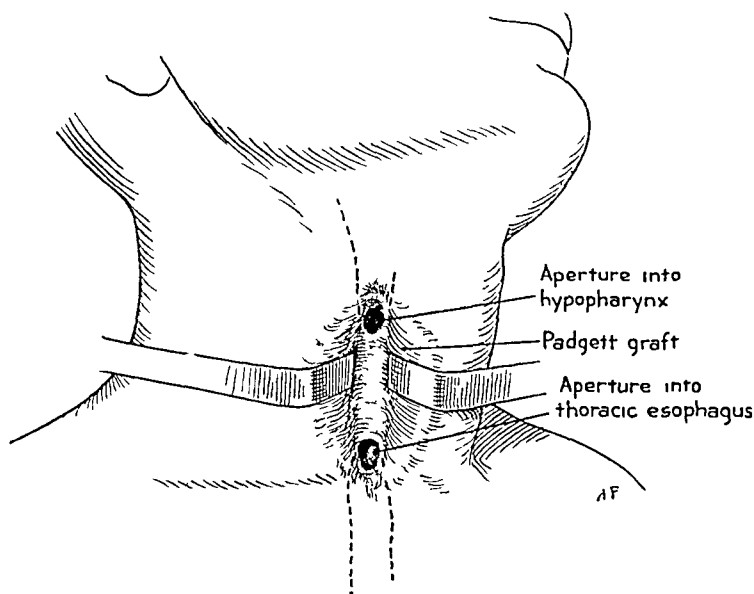


FIG 9 —Showing the new apertures into the pharynx and proximal esophagus



FIG 10 —Case 3. Apertures have been made in the upper and lower angles, and a string passed from the mouth down to, and through the gastrostomy stomi

wound, and the skin edges closed without tension over the tube. A full liquid diet was taken on the seventeenth day postoperative, and soon the patient was allowed a normal diet (Figs 12 and 13).

Comment —This patient had a very early cancer of the cervical esophagus developing in an area of leukoplakia, probably the result of chronic partial obstruction of thyroid origin. She is well only 18 months after excision of

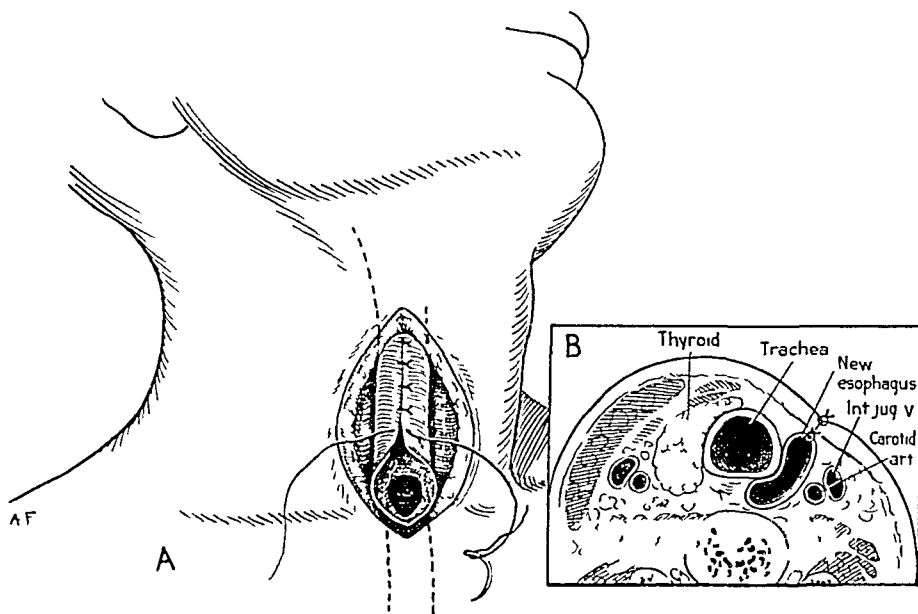


FIG. 11—Showing the formation of a new skin graft lined tube connecting the pharynx and the esophagus



FIG. 12—Photograph showing the patient after the final stage of the plastic closure

the esophagus, and time alone will determine whether or not she is cured of her cancer. One can only hope that stricture or rupture will not occur or an overgrowth of hair cause esophageal obstruction.

One patient with cancer of the cervical and upper thoracic portions of the esophagus was treated by gastrostomy and transthoracic and cervical esophagectomy in June, 1941. The patient made a surgical recovery, but it is too

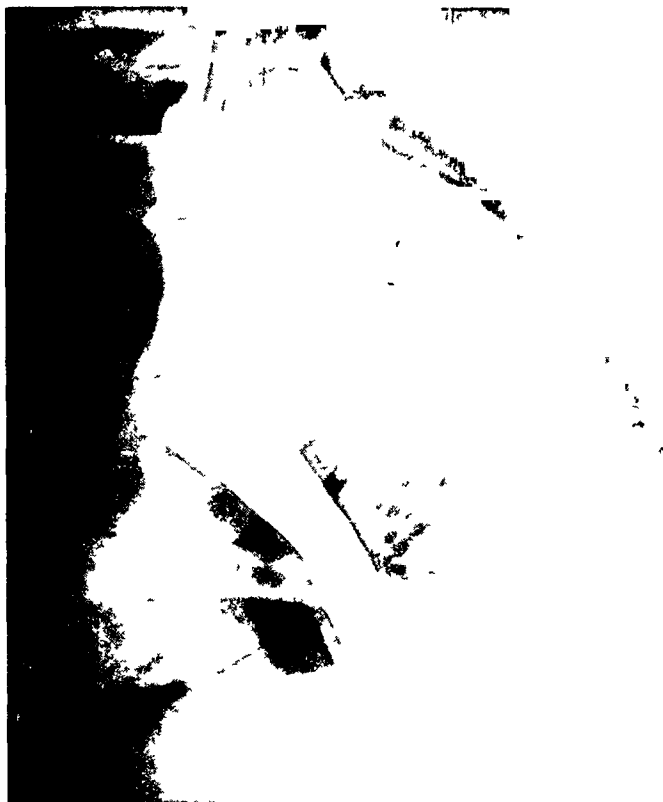


FIG. 13.—Case 3. Roentgenogram showing the reconstructed cervical esophagus after barium swallowing.

recent a case to warrant discussion as to the value of this procedure. However, it is safe to say that this approach allows the operator an opportunity of accomplishing a fairly wide tumor excision, and may do much to prevent the high recurrence rate noted in the literature.

SUMMARY

Cancer of the upper esophagus is shown to be a "curable" disease by radiation measures. A surgical approach to the disease, with a method of tubular reconstruction, is described in a detailed case report.

BIBLIOGRAPHY

- ¹ Ainscott, J. M. Case of Esophagotomy. *Med. Chir. Tr.*, 18, 86, 1833.
- ² Billroth, T. Über die Resektion des Esophagus. *Arch. f. klin. Chir.*, 13, 65-69, 1871.
- ³ Cheever, D. W. Two Cases of Esophagotomy for the Removal of Foreign Bodies, with some Remarks. 2nd ed., Boston, J. Campbell, 1868.
- ⁴ Cock, Edward. A Case of Pharyngotomy for Extraction of a Foreign Body, with some Remarks. *Guy's Hosp. Rep.*, 4, 217, 1858.
- ⁵ Czerny. Neue Operationen. *Zentralbl. f. Chir.*, 1877, pp. 433-434.
- ⁶ Eggers, C. Carcinoma of the Upper Esophagus and Pharynx. *ANNALS OF SURGERY*, 81, 695, 1925.

- ⁷ Evans, Arthur, quoted by Turner Recent Advances in the Treatment of Carcinoma of the Esophagus from the Surgical and Radiological Aspects Proc Roy Soc Med (Sect Laryngol), 27, 7-17, 1934
- ⁸ Goursauld, quoted by Cheever Two Cases of Esophagotomy for the Removal of Foreign Bodies, with some Remarks 2nd ed, Boston, J Campbell, 1868
- ⁹ Lane, W A Excision of a Cancerous Segment of the Esophagus Restoration of the Esophagus by Means of Skin Flap Brit Med Jour, 1, 16, 1911
- ¹⁰ Mikulicz, J Ein Fall von Resection des Carcinomatosen Esophagus mit Plastischem Ersatz des excidirten Stuckes Prag med Wchnschr, 11, 93, 1886
- ¹¹ Nielson, Jens Klinische Versuche zur Strahlenbehandlung des Speiserohrenkrebses Acta Radiol, 21, 352-367, 1940
- ¹² Roland, quoted by Cheever Two Cases of Esophagotomy for the Removal of Foreign Bodies, with some Remarks 2nd ed, Boston, J Campbell, 1868
- ¹³ Torek, F Carcinoma of Larynx, Pharynx, Trachea and Esophagus ANNALS OF SURGERY, 84, 889, 1926
- ¹⁴ Trotter, quoted by Pilcher, R Carcinoma of the Cervical Esophagus Lancet, January 9, 1937, p 73
- ¹⁵ von Bergmann, E Uber den Oesophagusdivertikel und seine Behandlung Arch f klin Chir, 43, 1-30, 1892
- ¹⁶ von Hacker, V Uber Resection und Plastik am Halsabschmidt der Speiserohre Insbesondere beim Carcinoma Verhandl d Deutsch Gellsch f Chir, Berlin, 37, 359-425, 1908

(Note—The discussions contain references to benign conditions of the cervical esophagus which formed a part of the original report as presented to the New York Surgical Society. These benign conditions have not been included in the paper for publication.)

DISCUSSION DR JOHN H GARLOCK (New York) said that there is a rather general agreement today concerning the surgical treatment of a pulsion diverticulum of the cervical esophagus. The only point for discussion is concerned with a one- or two-stage operation. Doctor Garlock believes that, in average hands, the two-stage procedure is a safer one and probably is most often utilized throughout the country.

With respect to cancer of the cervical esophagus, it has been the experience of most observers that the majority of these cases report for treatment after the tumor has become inoperable. Most of the patients that he had seen had been treated by radiation methods. The unusual result reported by Doctor Watson, in a male, age 70, can be attributed, in great part, to the low-grade malignancy of these tumors usually seen in the aged, and to the rapid response to radiation therapy. Most of these cases reported in the surgical literature have not survived more than one year.

With respect to the surgical treatment of carcinoma of the cervical esophagus, numerous methods have been devised, the most radical of which is that described by Eggers. In his operation, the larynx as well as the cervical esophagus is excised and a permanent tracheotomy is made in the supra-sternal notch. In early cases Doctor Garlock said he could visualize a radical resection without removal of the larynx, and Doctor Watson has demonstrated that this can be done. The idea occurred to Doctor Garlock, as Doctor Watson was describing the operation, that, at the time of the original mobilization of the organ, instead of fashioning a flap of skin and placing it beneath the exposed esophagus, thereby placing the esophagus under greater tension and jeopardizing its blood supply, it might be feasible to place a free split-thickness skin graft beneath the esophagus, epithelial surface forward, in order to form a skin-lined base for future aid in reconstruction. The pressure of the mobilized esophagus on the graft would facilitate complete "take" of the transplant. This maneuver would save many steps in the subsequent reconstructive process.

DR HOWARD LILIENTHAL (New York) said that in all his years of operating he could remember but a single case in which he dealt surgically with a pulsion diverticulum in the neck. In that case the opening into the esophagus was larger in diameter than that of the esophagus itself. When the diverticulum was full, the overflow entered the esophagus. The patient, a male, age 55, had been ill a long time, and was emaciated and weak. No gastrostomy was performed, but the procedure employed was one devised by another surgeon (Doctor Lilienthal thought by the late Doctor Freeman, of Denver). Through an incision in the left side of the neck the diverticulum was withdrawn and anchored with a ligature to the ear, so that the opening into the gullet was its lowest part and the sac was kept empty by gravity. There was immediate improvement and, in about three weeks, the second stage was performed. This consisted in the ablation of the sac and suture of the wound in the esophagus. The convalescence was stormy, and for a short time there was some slight leakage through the skin wound. Eventual and complete recovery followed, and Doctor Lilienthal had seen the man at intervals for a number of years. The case was reported before the New York Society for Thoracic Surgery, and published in the *Journal of Thoracic Surgery*, St. Louis, vol. 5, No. 5.

In regard to long-continued treatment by radiation, Doctor Lilienthal asked Doctor Watson if there might not be danger of epidermal malignancy. A number of years ago Doctor Lilienthal saw a patient who had been treated with radiation for goiter and there developed a quadrangular epithelioma, its area was that of the shield which had been used to confine the space treated by the rays. The patient was shown before the American Surgical Association.

DR WILLIAM L. WATSON (closing) said that Doctor Garlock's suggestion that a primary skin graft could possibly have been carried out at the original operation in the case of the lady with carcinoma of the cervical esophagus, was thought of at the time of operation, and that if he had to do it over again he thinks that is exactly what he would do. However, at the time of operation he had removed the sternocleidomastoid muscle, the right lobe of the thyroid gland, and the strap muscles, and that to have placed a skin graft behind the esophagus it would necessarily have had to be placed directly in contact with the common carotid artery and internal jugular vein, and there was some question in his mind whether a graft would have been successful under these conditions. The ideal arrangement would have been to have had a skin flap from the right side of the neck to cover the artery and vein, and a skin graft from the abdomen to place around the trachea and behind the mobilized esophagus.

The question of pulsion diverticulum of the esophagus, and the type of operation to be employed, comes up every so often, but with the newer chemicals and the newer surgical knowledge of the mediastinum the two-stage procedure will probably be used much less frequently in the future. The first patient upon whom Doctor Watson performed a two-stage procedure had a coughing attack the day following the first operation, so that the violent neck movements tore out the sutures which had been used to hold the sac in the upright position. The wound became infected, and the second stage of the operation was very difficult. Doctor Watson said it was his impression that the two-stage procedure is more apt to be followed by recurrence.

With regard to the question of late radiation effects in these patients with cancer of the cervical esophagus treated by radiation, the patient shown by Doctor Watson at this time is the only one who is alive more than five years. So far, he has not shown any tendency to develop postradiation complications. The other patients treated in this fashion have not lived long enough to develop the complications mentioned by Doctor Lilienthal.

CYSTS OF THE SPLEEN

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DETROIT, MICH

AND

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UNLIKE cysts of the ovary, liver, kidney or other abdominal organs, cysts of the spleen are very rare. Only four cases were reported by Pemberton² in approximately 800 splenectomies, an incidence of 0.5 per cent. Up to January 1, 1939, Fowler¹ collected a total of 137 reported cases. We have found 11 more reported in the literature,²⁻¹¹ up to February 1, 1941, making a total of 148. We wish to report an additional case seen recently at the Henry Ford Hospital.

Cysts of the spleen have been classified as single or multiple, unilocular or multilocular, parasitic or nonparasitic, true or false, primary or secondary, and hemorrhagic, serous, or lymphatic. Most of these classifications are not entirely satisfactory. The following classification (Table I) is a modification of those submitted by Moynihan^{1,2} and Fowler.^{1,3} True cysts of the spleen have a specific secreting lining which may be epithelial, endothelial, or parasitic. False cysts possess only a dense hyaline fibrous tissue wall or a layer of condensation of adjacent splenic tissue.

TABLE I
CYSTS OF THE SPLEEN

- I True cysts—lined by specific secreting membrane
 - A Epithelial
 - 1 Dermoids
 - 2 Epidermoids
 - B Endothelial
 - 1 Lymphangioma
 - 2 Hemangioma
 - 3 Polycystic disease
 - 4 Some serous cysts
 - C Parasitic—lined by protoplasmic matrix containing numerous nuclei
 - 1 Hydatid cyst caused by *echinococcus*
- II False cysts—no specific secreting lining
 - A Hemorrhagic
 - B Serous
 - C Inflammatory
 - 1 Acute necrosis in infection
 - 2 Chronic tuberculosis
 - D Degenerative liquefaction of infarcted areas caused by embolism or arterial thrombosis

According to Fowler,¹ *echinococcus* cysts occur about twice as frequently as all of the various forms of nonparasitic cysts. False cysts are encountered approximately four times as often as the true type. Eighty per cent of the false cysts are large, solitary, and unilocular, two-thirds being of the hemorrhagic variety, and one-third of the serous type. An additional case report of a large, solitary false serous cyst of the spleen is presented herewith.

Case Report—J S, white, male, age 11, was admitted to the Henry Ford Hospital, March 2, 1940, complaining of pain and fulness in the left abdomen. He had been well until three months previously, when a bulging of the upper left abdominal quadrant was first noted. There was no history of abdominal trauma preceding the appearance of this mass. Two weeks prior to his admission to the hospital, the bulging area became painful, following a blow by the handle of a snow shovel. The past history was essentially negative.

Physical examination revealed a well-nourished white boy who did not appear acutely ill. Temperature 99.2° F, pulse 88, respirations 20. The head, neck and chest

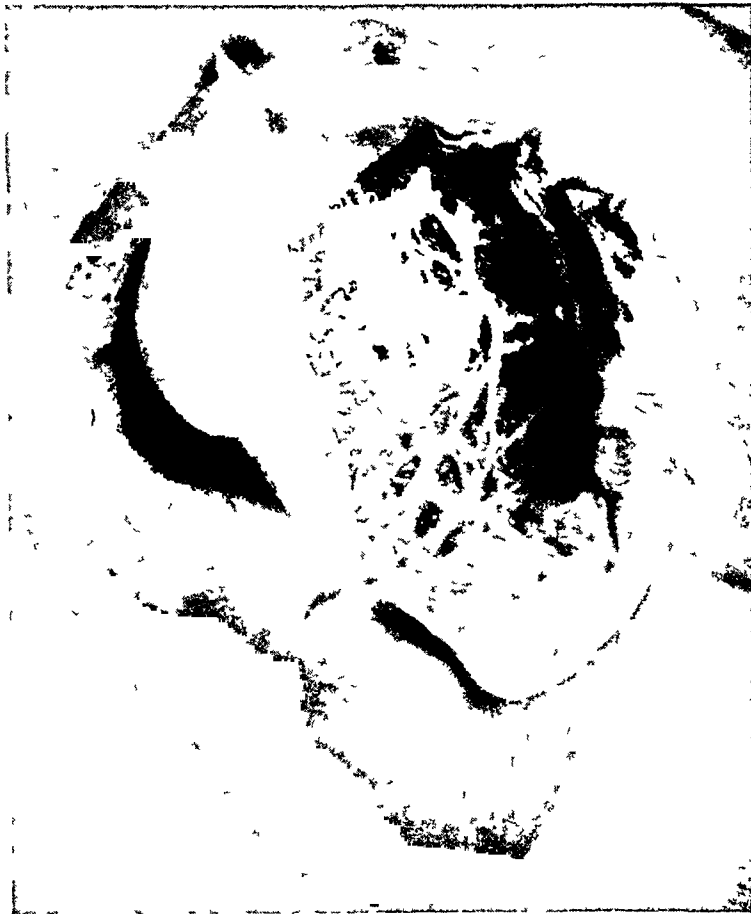


FIG. 1.—The gross appearance of the removed spleen.

were essentially normal. In the left upper quadrant of the abdomen a definite bulging was evident. Percussion note over this area was flat. A large mass was palpated extending inferiorly and medially from beneath the left costal margin. It was smooth, rounded, firm, slightly tender and moved with respiration. No notch was palpable. Rectal examination was negative. Urinalysis showed no abnormal findings except a positive reaction for albumin. Hemoglobin 11.7 Gm, RBC 4,070,000, WBC 5,250. Differential count showed no significant changes. The tuberculin and blood Wassermann tests were negative. A plain roentgenogram of the abdomen showed a large soft tissue tumor in the left upper quadrant, which extended inferiorly and slightly to the right of the midline. Barium enema examination revealed downward and forward displacement of the splenic flexure of the colon by an extrinsic mass. Pnelograms showed upward displacement of the left kidney.

Operation—March 7, 1940. A left subcostal incision revealed a large splenic cyst occupying the upper two-thirds of the spleen. It contained 1,620 cc. of straw-colored

fluid After aspiration of the fluid, the spleen was mobilized by separating its adhesions to the diaphragm and posterior parietal peritoneum Splenectomy was then performed after division of the gastrosplenic ligament and transfixion of individual vessels in the pedicle by black silk The patient withstood the operative procedure very well, and his wound healed *per primam*

Pathologic Examination—Dr F W Hartmann The spleen weighs 270 Gm (after aspiration of contents of cyst), and measures 17.5×12.0×7.0 cm The lower third of the spleen is of normal consistency with light reddish-brown color, and distinct architectural markings The upper two-thirds consists of a thin-walled cystic structure, with a maximum diameter of 13 cm Trabeculations are present within the lumen (Fig 1) On the cyst wall, enlarged cords of fibrous tissue run in all directions Microscopic examination of sections of the spleen and cyst wall shows the latter to be devoid of epithelial lining The wall consists of rather dense, pink-staining, fibrous tissue, beneath which there is considerable bloody extravasation The adjacent splenic tissue appears normal *Pathologic Diagnosis*—Benign simple cyst of spleen

Discussion—The solitary nonparasitic cysts of the spleen is the type most frequently encountered by the surgeon In the series of 137 cases, collected and reported by Fowler,¹ 79 per cent, or 108 cases, were of the false variety Of these 108, 71 per cent, or 77 cases, were large solitary hemorrhagic cysts, and 29 per cent, or 31 cases, were large serous cysts The present case falls into this latter group

The etiology of solitary nonparasitic splenic cysts is still obscure It has been repeatedly pointed out that too few cases have been reported to justify any extensive conclusions as to etiology Women appear to be most often affected, particularly during the child-bearing age Most cases occur between the ages of 20 and 50, although they have been noted in very young children and even in the newly born infant Trauma seems to play an important rôle in the formation of large hemorrhagic or serous types Many of these are more properly described as encysted hematmata due to an injury which fails to produce a laceration of the surface of the spleen, but which causes tearing of the vessels in the interior of the organ and gross hemorrhage If the patient survives, a cyst with bloody-stained fluid and fibrous walls is formed in time Intrasplicenic hemorrhage, however, may also occur spontaneously without antecedent trauma and subsequently form a cyst

It is believed by some that the complete absorption of blood results in the transformation of a hemorrhagic cyst to a serous type, although it is known that the majority of cases of serous cyst give no history of previous trauma In Fowler's series only 16 per cent of the serous type were known to have been preceded by trauma

The signs and symptoms of splenic cyst are not distinctive Since no apparent function of the adult spleen is known, we are unable to recognize any symptoms attributable to the involvement of the splenic pulp itself When the cysts are small, there are no symptoms, when they are large, symptoms may result secondarily from adhesions or pressure upon adjacent organs The chief of such pressure symptoms is pain, characterized by a dragging sense of heaviness in the left hypochondrium and epigastrium Occasionally the pain may be referred to the left shoulder Digestive disturbances such as nausea,

vomiting, flatulence and constipation have been frequently observed. Rarely, a twisted splenic pedicle has resulted in collapse. Usually the surgeon is consulted, not because of symptoms, but because of a mass in the abdomen.

The diagnosis of splenic cyst is very difficult. The location of the tumor usually suggests splenomegaly, but the cystic nature is generally not recognized until the organ has been exposed. Cyst of the spleen must be differentiated from other causes of splenomegaly, and cystic disease of the pancreas, omentum, mesentery, left lobe of liver, ovary, or kidney. Roentgenologic examination is of great help. A large soft tissue mass may be seen on the plain film associated with elevation of the diaphragm, bulging of the left lower intercostal interspaces, obliteration of psoas shadow (Ostro and Makover¹⁴), and, occasionally, displacement of kidney. After a barium meal, the stomach may be seen pushed to the right. Barium enema examination will show downward displacement of the splenic flexure. If a preoperative diagnosis of splenic cyst is made, it must be differentiated from the echinococcal type. This differentiation may be possible by the precipitin test of Welch and Chapman, the complement fixation test of Weinberg and Pavu, and the cutaneous allergic test of Casoni.

Treatment—Only cysts of relatively large size require treatment, and fortunately these are usually readily amenable to surgery. Splenectomy, which gives a mortality rate of only 4 per cent,¹ is the treatment of choice, and is usually possible in the nonparasitic solitary type. Enucleation of the cyst is rarely feasible, but has been accomplished. The difficulty in controlling hemorrhage makes it a more dangerous operation than splenectomy. Malsupialization results in a prolonged postoperative course and should be rarely necessary in this type of cyst. Incision and drainage, in one or two stages, has been performed, particularly in those instances when splenectomy was considered too hazardous or impossible.

SUMMARY

A short discussion of cystic disease of the spleen in general and of false cysts in particular is given. The case history and pathologic description of an additional case of a false serous cyst is reported.

REFERENCES

- ¹ Fowler, R. H. Cystic Tumors of the Spleen. *Int. Abstr. Surg.*, **70**, 213, 1940.
- ² Roberson, F. Solitary Cysts of the Spleen. *ANNALS OF SURGERY*, **111**, 848, May, 1940.
- ³ Sherwin, B., Brown, C. R., and Libei, A. F. Cystic Disease of Spleen. *ANNALS OF SURGERY*, **108**, 615, April, 1939.
- ⁴ Lerchboullet, P., Gregoire, R., Benard, J., and Ibarran, R. Epidermoid Cysts of Spleen. *Sang*, **13**, 853-869, 1939.
- ⁵ Pisa, V., and Sikl, H. Nonparasitic Cysts of Spleen. *Deutsche Ztschr. f. Chir.*, **252**, 746-755, 1939.
- ⁶ Bergan, F. Solitary Cyst of Spleen. *Nord. Med.*, **1**, 307-310, February, 1939.
- ⁷ Filho, A. P. Cysts of Spleen. *Hospital, Rio de Janeiro*, **15**, 595-604, March, 1939.
- ⁸ Cabot, H. Splenic Cyst. *New England Jour. Med.*, **222**, 1052, June 20, 1940.
- ⁹ Watts, T. D., and Warthen, H. J. Nonparasitic Cysts of Spleen. *South. Surg.*, **10**, 34-38, January, 1941.

- ¹⁰ Mason, A Unilocular Cyst of the Spleen Australian and New Zealand Jour Surg, **10**, 304-305, January, 1941
- ¹¹ Andrews, F T, and Horter, R S Solitary Cysts of Spleen Jour Michigan Med Soc, **38**, 201, 1939
- ¹² Moynihan B Cysts of the Spleen Surg, Gynec, and Obstet, **40**, 778, 1925
- ¹³ Fowler, R H A Pathological and Surgical Study ANNALS OF SURGERY, **57**, 658, 1913
- ¹⁴ Ostro, M, and Makovei, H B Nonparasitic Cyst of Spleen with Special Reference to Roentgenological Aid in Diagnosis Am Jour Roentgenol, **37**, 782, June, 1937

HEMORRHAGIC CYST OF THE SPLEEN

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THE SPLEEN is unique in that it is a prominent and predominating factor in a very large number of blood dyscrasias and other pathologic processes and clinical entities.

It is the purpose of this paper to discuss a rare variety of splenic cyst, that is, large solitary hemorrhagic cyst. Cysts of the spleen have been classified by Fowler,^{1, 2} as dermoid, parasitic, and nonparasitic cysts. Nonparasitic cysts may be subdivided into (1) True cysts, and (2) pseudocysts. The true cysts include (1) Infestation cysts, which are inclusions of peritoneum— inflammatory or traumatic, small and multiple—may be superficial or deep. (2) Dilatation cyst or polycystic disease of the spleen. (3) Neoplastic types (lymphangioma, hemangioma). Pseudocysts have two subdivisions. (1) Traumatic, which may arise from a hematoma, and are usually large and unilocular (hemorrhagic and serous cysts—so called from their contents). (2) Degeneration cysts arising from secondary changes in infarcted areas from arterial degeneration or occlusion of blood vessels by emboli with consequent necrosis of the spleen pulp, these are also usually solitary and large. It is with this last mentioned class, that is, pseudocysts, or large solitary hemorrhagic cysts, that this paper deals. These cysts have no true cyst lining. Baccelli indicated that cysts could arise from hematomata, and that a capsule could form about them with a special inner cell lining, and that, as a result, it would not be possible to distinguish them from lymph cysts into which there had been hemorrhage.

Lubarsch disagreed, and believed that no true cell lining could form in a hematoma of the spleen. The genesis of cystic spleen seems to have no points of analogy to the genesis of cysts of the ovary and kidney. In the absence of tubular structure, true retention cysts do not occur.

That hemorrhagic cysts of the spleen are rare is attested to by Benton,³ who, in 1932, brought the reported number up to 96. The rarity of this condition is further evidenced by the fact that examination of the records of Bellevue Hospital, from 1904 to date, reveal no case of hemorrhagic cyst of the spleen. The only case at all resembling it was a large lymphangioma. Examination of the Pathology Department and mortuary records at Bellevue revealed, for the period from 1904 to 1940, eight cases of cyst of the spleen. It is interesting to note that during this same period there were 48 cysts of the liver. Of these eight cystic spleens, four showed small multiple infestation cysts, one, a cavernoma with cyst, one, a small unclassified cyst, one, a small parasitic cyst, and one, a small calcified cyst. A study of the records of St. Vincent's Hospital, during the 30 years prior to 1940, revealed no case of

hemorrhagic cyst of the spleen In this paper will be presented five additional cases from the New York Post-Graduate Hospital

In the majority of the cases previously reported, the disease has affected persons in middle adult life—a fairly good argument against congenital origin About two-thirds were females, so the majority of cases occurred in women during the child bearing age Monnier explains the predilection for the occurrence during the reproductive period of women, by the fact that the spleen becomes congested in pregnancy, during menstruation, and at the menopause, and subsequently relaxes Large spleens are more apt to be injured and so we find malaria and syphilis predisposing diseases The one generally acknowledged factor is trauma, reported in about 30 per cent of the cases

CASE REPORTS

Case 1—J D, female, age 42, married No present or past history is available at this time except that there was no history of trauma Roentgenograms, destroyed some time ago, showed a cyst of the left upper abdomen, there being a dense ring of calcified tissue about the cyst The urine and blood count were normal On July 1, 1919, at the New York Post-Graduate Hospital, Dr John F Erdmann performed a splenectomy for a large, solitary, hemorrhagic cyst She had an uneventful convalescence, and was discharged on the eighteenth postoperative day

Case 2—M H, female, age 12, gave a history of a fall two years prior to admission, in which fall she struck her left upper abdomen Her past history included measles and pertussis On physical examination of the abdomen, one found a mass over one handbreadth below the left costal margin The urine and blood count were normal The speaker was present in the operating room when Dr John F Erdmann performed, on May 25, 1928, at the New York Post-Graduate Hospital, a splenectomy for a large solitary hemorrhagic cyst of the spleen The diagnosis made by the pathologist was a "solitary hemorrhagic cyst of the spleen with fibrosis of the spleen and chronic fibrous perisplenitis probably due to trauma" Convalescence was uneventful, she left the hospital on the fifteenth postoperative day Doctor Erdmann has seen, or heard from her annually for these past 12 years, and she is well

Case 3—M B T, female, age 28, unmarried, was admitted to the New York Post-Graduate Hospital, with the chief complaints of pain in the right lower quadrant and the left abdomen of one year's duration Her past history included a tonsillectomy 13 years previously, and frequent attacks of influenza For one year prior to admission, the patient had had dull pains in the right lower quadrant, varying in intensity, and sometimes absent She had occasional nausea when tired There had been occasional pain in the left abdomen, worse following roentgenotherapy five months previously She had noticed a mass in the left abdomen for 16 years, but no pain or tenderness in that region until one year previously

The urine and blood count were normal A large, firm, movable mass could be felt in the left upper quadrant, extending well over to and below the umbilicus At operation, Dr John F Erdmann removed the spleen containing a large, solitary hemorrhagic cyst and a cystic right ovary This patient had an uneventful convalescence, and was discharged on the twentieth postoperative day

Case 4—M K, male, age 23, was admitted to the New York Post-Graduate Hospital, with the chief complaint of a "mass in the abdomen" of four years' duration His past history was not remarkable, he had had the usual childhood diseases The relevant facts of present illness were that four years prior he had noticed a bulge in the left upper abdomen and a small mass, freely movable and not tender Three months before

hospitalization, he had noted a gradual increase in the size of the mass, so progressive that his vest no longer fitted him. He had no symptoms whatever.

Physical examination revealed a mass four finger's-breadth below the left costal margin, the mass was movable, lobulated, and felt like encapsulated fluid rather than a solid tumor. The stomach was found pushed to the right. Intravenous urograms showed fairly good left kidney function, the minor calices were not visualized. A retrograde left pyelogram showed the mass to be not part of the kidney, and probably splenic.

Laboratory data indicated normal urine and blood counts, normal nitrogen, chloride and CO_2 combining power blood values, and a negative complement fixation for *ecchinococcus*.

On October 26, 1932, Dr. C. G. Heyd removed the spleen. There was at the lower pole of the spleen a cyst, containing 2,000 cc of chocolate-colored material, it was ten inches in diameter, there were adhesions of the omentum and intestine. The pathologist reported "benign cyst of the spleen, hypoplasia of the spleen, no true cyst lining."

Postoperatively, the patient did well and left the hospital on the fifteenth day.

Case 5—(Author's case) The patient, a male, age 32, was admitted to the New York Post-Graduate Hospital, complaining of intermittent, dull pain in the left upper quadrant of eight months' duration. There was, he said, a feeling of something sticking to the anterior abdominal wall on inspiration, suddenly released on expiration. He complained, moreover, of slight gas eructations.

Twenty-four years prior to admission he had suffered a fracture of the right leg, for ten years he had noticed a prominence in the left upper quadrant, symptomless until eight months prior to his coming into the hospital.

Abdominal examination showed a firm mass in the left abdomen, extending almost to the umbilicus below and medially, medially there was a notch, the mass moved with respiration. Gastro-intestinal roentgenologic studies showed "some diverticula pouching in the pars cardia under the dome of the diaphragm near the midline", and showed a large extragastric mass displacing and compressing the stomach to the right (Figs 1 and 2). Intravenous and left retrograde pyelograms showed extrinsic pressure on the left kidney (Fig 3).

The laboratory reported the urine as having a little albumin, and five granular casts, per high-power field, blood Wassermann was negative, basal metabolic rate was minus one, icterus index seven point nine, hemoglobin 88 per cent, R B C 4,600,000, W B C 3,000 to 6,000, with a normal differential count, and normal fragility of erythrocytes.

On December 9, 1937, a diagnostic splenic puncture was made. Dark green fluid spurted from the needle, this showed innumerable cholesterol crystals.

On December 13, 1937, four days after splenic puncture, under ether anesthesia, the spleen was removed. There was a large cyst at the upper pole. Convalescence was uneventful and the patient was discharged on the thirteenth postoperative day.

Pathologic Report—Gross The spleen, which weighs 1,110 Gm, after perfusion and fixation, is enlarged and distorted by a cystic condition of one pole. The cystic area measures approximately $14 \times 13 \times 12$ cm. The noncystic portion surmounts the cystic portion, in the manner that the epididymis surmounts the testis. The solid portion has maximum diameters of 15, 6 and 4 cm (Fig 4).

The capsule of the spleen shows distinct confluent areas of gray thickening, particularly over the cystic portion. These stand out in map-like fashion, against the background of normal brown red. At the hilus the vessels are normal in appearance.

On section, about 500 cc of freely flowing chocolate-colored, slightly frothy fluid escapes. On standing fresh blood settles. The cyst wall has an average thickness of one mm for the most part where there is practically no splenic tissue in its wall. At the junction with the unaltered spleen the thickness increases because of the thin lamella of splenic tissue included (Fig 5).

The cyst wall is the gray tissue of the spleen capsule except where the splenic tissue is noted. The inner lining is shaggy. It is dark brown-red where splenic tissue lines the cyst and slightly dirty golden yellow where the splenic capsule serves as the cyst capsule. There are numerous incomplete septa formed by the fibrinous elements.

The noncystic portion of the spleen is separated from the cystic areas only by the lining of clot already described. This finding further strengthens the belief that the

FIG 1

FIG 2

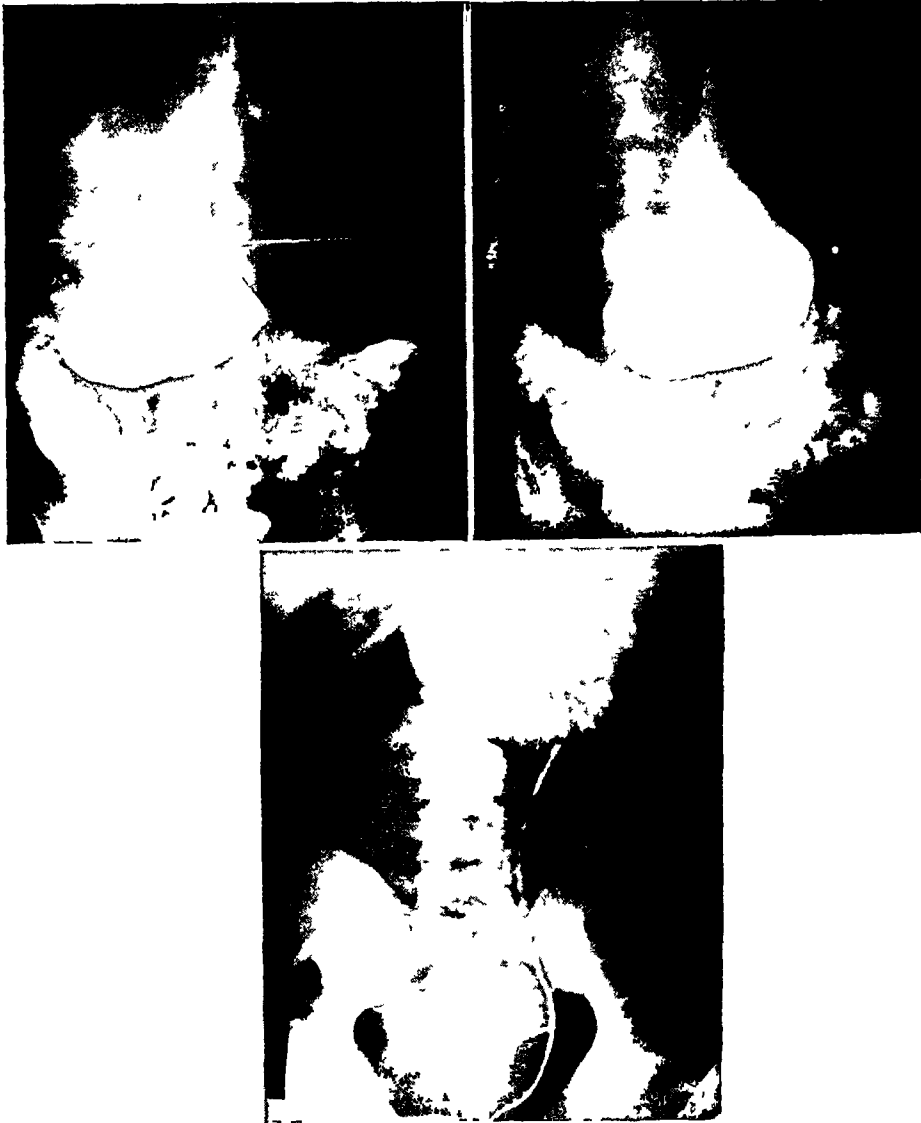


FIG 3

FIG 1—Roentgenogram showing a mass in the left upper quadrant displacing the stomach to the right and the intestines below.

FIG 2—Oblique roentgenogram showing the mass in the left upper quadrant and the displacement of stomach and intestines.

FIG 3—Left retrograde pyelogram showing an essentially normal left kidney.

major portion of the wall of the cyst is the splenic capsule and that the cyst probably arose as a result of a breakdown of a large hematoma.

Microscopic—The unaltered portion of the spleen is free of blood, because of the perfusion fixation. There is normal delicate structure to the sinuses which are lined by endothelial cells. There are no signs of sclerosis either in the capsule in such areas or in the splenic arteries or arterioles.

The capsule of the spleen can be traced outward where it forms the wall of the cyst. Here the cyst is lined by a layer of eosinophilic amorphous material in which there are numerous spear-shaped spaces, cholesterol crystals.

In those portions of the cyst where the wall is formed by the adjacent spleen the cholesterol crystal-bearing amorphous material is in part replaced by granulation tissue which is separated by more mature connective tissue from the spleen proper. Many of the cells of the granulation tissue are swollen, with fine light yellow-brown material, phagocytized lipids. Fresh areas of hemorrhage are also noted in the granulation tissue.

Pathologic Diagnosis Cyst of spleen apparently resulting from breakdown and organization of repeated hemorrhages.

This patient has been seen every few months since operation. He is symptom-free and well. Blood counts, made every three months, have been normal, averaging a hemoglobin of 90 per cent, RBC 4,800,000, WBC also normal, the blood smears are normal.



FIG. 4—Left lateral view of the spleen.



FIG. 5—View of the cut spleen showing the large cyst in the upper pole. The cyst is about one fifth the size before decompression.

SUMMARY—The clinical picture of these five cases is strikingly similar, namely, a firm mass in the left upper quadrant, extending to the midline and down to the umbilicus, the general health and condition of the patient unaffected, some discomfort in the left upper quadrant and moderate indigestion, rather normal blood counts with no evidence of any blood dyscrasia, gastro-intestinal roentgenograms, when made, showing an extragastric mass pressing the stomach to the right, left pyelogram showing no intrinsic kidney lesion.

Five cases of solitary, large hemorrhagic cyst of the spleen are reported. All presented the same clinical picture and all were cured by splenectomy.

My thanks are due to Doctors Erdmann, Heyd and Symmers for use of material.

REFERENCES

- ¹ Fowler, R. H. Cysts of the Spleen. *ANNALS OF SURGERY*, 57, 658-690, January, 1913.
- ² Fowler, R. H. Surgery of Cysts of the Spleen. *ANNALS OF SURGERY*, 74, 20-36, July, 1921.

³ Benton, R W Large Cysts of the Spleen J A M A, 99, 1674-1676, November 12, 1932

DISCUSSION DR CHARLES GORDON HALL (New York) On June 26, 1939, I reexamined the fourth case quoted by Doctor Denneen, and found the patient in excellent health, with a firm abdominal cicatrix

Dr Royal H Fowler, and from whom I quote freely, in March, 1940, made his latest contribution on cystic tumors of the spleen (International Abstract of Surgery, Surg, Gynec, and Obstet, 70, No 3, March, 1940) From the first cystic tumor of the spleen, a dermoid reported by Andral, in 1829, to January 1, 1939, Fowler reports from the literature 137 nonparasitic splenic cysts, 21 per cent being primary or true cysts, and 79 per cent secondary or false cysts Doctor Denneen now adds five additional cases, three of Dr J F Eidmann, one of Doctor Heyd, and one by himself It is obvious that there must be a considerable number of unreported cases—occasions where the surgeon encounters one case and does not report it In any event, solitary cysts of the spleen are uncommon when compared with the incidence of parasitic cysts (echinococcus 2 per cent in the spleen) or with cysts of ovary, liver or kidney Secondary splenic cysts (79 per cent) are about four times as frequent as primary cysts (21 per cent)

Polycystic disease, lymphangiomata and hemangiomata constitute 62 per cent of the 21 per cent of primary, true splenic cysts, the remaining 38 per cent being dermoid and epidermoid cysts Eighty per cent of the secondary or false cysts are large solitary hemorrhagic cysts, as indicated by Doctor Denneen Of these, 35 per cent lie deep within the interior of the spleen and 65 per cent somewhat subcapsular

Various theories have been advanced to account for hemorrhagic cysts of the spleen, *viz*

(1) Effect of menstruation and pregnancy Seventy per cent of the splenic cysts that occurred in pregnancy were large, solitary hemorrhagic cysts Fowler believes that the most rational explanation of the development of cysts of the spleen following pregnancy is that infarction and secondary hemorrhage with cyst formation follows an embolism

(2) Trauma is an alleged factor in 25 per cent of the cases Eighty per cent of the cases in which trauma was elicited had large solitary hemorrhagic cysts

(3) Antecedent disease Malaria present in 74 per cent of all of Doctor Fowler's series, 11 per cent had syphilis, and 52 per cent associated with previous disease had a unilocular cyst with hemorrhagic contents

Thus trauma and antecedent disease, one or the other, or both, were noted in the history in all the cases of unilocular hemorrhagic cyst of the spleen

URINARY EXTRAVASATION (PERIURETHRAL PHLEGMON)

A CLINICAL STUDY OF 32 CASES

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IN A previous communication⁵ the anatomy, bacteriology, and pathogenesis of urinary extravasation were reviewed. The superficial perineal pouch of Colles,⁴ in cadavers, was injected with radiopaque colored fluid, the amounts and pressures were recorded, and, subsequently, serial roentgenographic demonstrations and dissections were made. The following conclusions were derived from these studies and experiments:

(1) Anatomically, Colles' fascia is so disposed as to allow of a progressive urinary infiltration of the perineum, scrotum, penis, groins, and anterior abdominal wall.

(2) Injection experiments reveal that the clinical appearances can be simulated (with the exception of penile and abdominal involvement) by using pressures and amounts of fluid comparable to those expected on voiding.

(3) Urine alone does not suffice to produce the clinical pictures.

(4) Other factors are operative in the living subject, namely, (a) the presence of bacteria, (b) the tonicity, contractility and elasticity of the tissues, and (c) an active circulation.

(5) Injection experiments demonstrate the ease with which the vascular tree is inadvertently entered.

(6) The close proximity of the vascular tree to the urethra permits of the easy development of vascular thrombosis or pressure phenomena from encapsulated fluid or abscess.

(7) Vascular thrombosis or infectious thrombophlebitis probably accounts for the frequency of rapid swelling of the genitalia, rapid gangrene, severe toxemia and jaundice.

(8) Injection experiments controlled by roentgenography and dissection, together with clinical and autopsy records, fail to show any case wherein the tunica vaginalis testis is involved by the extravasation.

Anatomic study reveals that all periurethral inflammations must penetrate the very vascular bulb or part of the spongiosum to reach the superficial perineal pouch. In this passage, from urethra to fascial space, they invariably involve the vascular tree, thereby easily setting up thrombosis or thrombophlebitis. Anterograde or retrograde extension of this process is favored by the contractions of the bulbocavernosus and external sphincter muscles, which are brought into play with each act of voiding. This explains the paradox wherein the condition of extravasation is aggravated in those cases which continue to void. Moreover, this concept of the pathogenesis explains the

development of extravasation or perimeethial phlegmon without stricture or obstruction, and also the urgent necessity for diversion of the urinary stream, irrespective of whether the patient is voiding well or not. These muscles must be put at absolute rest to prevent them from squeezing the thrombosed bulb, and thereby propelling the process into the scrotal and penile vessels.

On the other hand, according to the hydrostatic theory for the production of urinary extravasation, diversion of the urinary stream was practiced to prevent more urine from being squeezed out into the tissues through a defect in the urethra. This concept is not as sound as the former explanation. In accordance with this latter premise, many surgeons and urologists have failed to divert the urinary stream in cases which were voiding well, or which presented no stricture. The omission of urinary diversion has led to an unwarranted and high mortality.

Once extravasated urine, blood, or an abscess occupies the superficial perineal pouch, it is easy to see how the pressure of the mass in the confined space would produce vascular obstruction of the scrotal vessels without actual thrombosis. This mechanism is seen in many perimeethial abscesses. When the abscess is incised, the edema disappears, because of the release of pressure. This process is exemplified in Figure 4.

CLINICAL ASPECTS

Etiology and Symptoms—At the Harlem Hospital, New York City, most of the patients are Negroes. The high incidence of gonorrhea with its complications of stricture and perimeethial abscess, neglect, and unwarranted and unskillful instrumentation are the factors which combine to make extravasation more common than in other institutions.

TABLE I
RACE AND AGE INCIDENCE

Total number of cases	32
Number of white patients	4
Number of colored patients	28
Average age of all cases	44 7 yrs
Average age of 16 survivors	39 3 yrs
Average age of 16 fatal cases	50 2 yrs

TABLE II
FACTORS IN ETIOLOGY

	Number of Cases
History not obtained	4
No genito urinary symptoms voiding well	6
Stricture of urethra found by instrumentation operation or autopsy	19
Urethral instrumentation for stricture urinary retention or urethral stone	9
Trauma other than urethral instrumentation	2
Urethral stone removed by external urethrotomy	1

When a patient with extravasation is admitted to the hospital, the chief complaints are usually referable to toxemia. Chills, fever, malaise, and prostration are the symptoms which cause the patient to seek admission, and the

local signs and symptoms may be so minimal, that valuable time is often lost before the true nature of the condition becomes evident. As the toxemia increases, and especially when there is associated urinary retention, hiccough, disorientation, delirium, and stupor, coma rapidly supervenes. These cases commonly present icterus, which was present in eight of our series of 32 cases.

The most important factor in etiology was stricture, which was found in 19 cases of this series. Nine cases had had urethral instrumentation, two cases suffered trauma other than urethral instrumentation, and one case had a urethral stone. Six cases were voiding well and presented no genito-urinary symptoms on admission.

Of 20 wound cultures two were negative, and 11 presented mixed organisms which were found in the following incidence:

TABLE III
BACTERIOLOGY

Type of Organism	Number of Cases	Lived	Died
Gram-positive cocci	8	3	5
Staphylococci	7	6	1
<i>Streptococcus gamma</i>	1	1	0
Nonhemolytic streptococcus	1	1	0
Gram-positive bacilli	1	0	1
Gram-negative bacilli	4	2	2
<i>Bacillus coli</i>	6	3	3
<i>Bacillus proteus</i>	2	1	1
Gram-negative diplococci	1	0	1
Gonococci	1	0	1

Of the 32 cases analyzed blood cultures were negative in 15 cases, of which eight survived and seven died. There were two positive blood cultures. Case 21 presented *B. coli* and pneumococcus, and he died. Case 26 presented streptococcus *beta*, and he survived.

Although a history of antecedent gonorrhea, with frequency, dysuria, urgency, and gradually diminishing urinary stream, may be elicited in rational patients, all of these symptoms may be absent in insidious cases. Careful questioning usually elicits a history of long-standing urethritis or stricture. Superimposed upon either of these two conditions, one finds the situation recently altered by the advent of perineal abscess or trauma incident to urethral instrumentation or "straddle" injury. However, the onset of perineal abscess may be very insidious, and not until it is associated with urinary retention, severe toxemia, or frank extravasation is the patient forced to enter the hospital.

According to the hydrostatic theory for the production of urinary extravasation, the following explanation is advanced for the paradox that the worst cases encountered are those who continue to void: (a) Attention is not directed to the necessity for diversion of the urinary stream, because of the absence of retention. (b) If abscess, stricture, or rupture of the urethra produces complete retention, extravasation may not occur (and diversion is practiced early). (c) However, when abscess, stricture, or rupture of the urethra

does not completely shut off the urinary stream, extravasation may occur, and the increased hydrostatic pressure necessary to overcome the obstruction may force urine into the tissues at the site of the defect in the urethra.

Cystometrically, the normal expulsive pressure on voiding has been found to be between 60 and 80 Mm Hg. With irritative lesions, a hypertonic bladder is characteristic, and the pressure on voiding still higher. The pressure required in most of the injection experiments was usually also between 60 and 80 Mm—so that the hydrostatic theory for the infiltration of the superficial perineal pouch and the scrotum seems to be confirmed.

Since the patient has been straining for a long period of time, he may not be aware of any added effort. He may not complain of any urinary dis-



FIG. 1



FIG. 2

FIG. 1—Front and side views in a case of extravasation of urine at an early stage of the infiltration of the scrotal tissues. (After Lisendrath and Rolnick.) Note the huge swelling of the scrotum which is *symmetrical and continuous* with that of the perineal and suprapubic regions.

FIG. 2—Marked perineal and penile involvement with the scrotum "skipped" in a case of extravasation. Although scrotal involvement is present in this case, it is not as advanced as is usually observed on admission to the hospital. (After Campbell.) The swelling of the penis may have resulted from one of three factors: (1) Independent involvement of Buck's fascial compartment, (2) edema from pressure of the perineal mass, or (3) thrombophlebitis.

turbance. It has been the experience of the writer that the most treacherous cases, and those which were most mishandled, were those who continued to void. It did not occur to the surgeons caring for these patients that diversion of the urinary stream was essential to successful treatment. However, this is the most important part of the treatment, and success in handling these cases demands recognition of these facts.

According to the hydrostatic theory, voiding "squeezes" more urine out into the tissues, so that diversion is practiced. However, according to the new concept, voiding "squeezes" the thrombosed bulb of vessels and thereby propels the thrombophlebitic process, so that diversion is practiced to put the muscles completely at rest. Whichever concept we select, the urgent need for diversion of the urinary stream is seen as the most rational part of the treatment.

LOCAL CONDITION AND DIFFERENTIAL DIAGNOSIS

The swelling and inflammatory changes usually spread with great rapidity from an initial tender and edematous swelling in the midline of the perineum, leaving gangrene of the subcutaneous tissues in its wake. One most fre-

quently encounters a swelling in the perineum associated with a continuous, symmetrical swelling of the scrotum and penis, and later, sometimes, involvement of the groins and lower abdomen (Fig 1) Occasionally, the scrotum is "skipped," when the perineum is the site of a swelling and the penis is markedly swollen as a result of the involvement of Buck's¹ fascia independently of Colles' pouch or as a result of thrombophlebitis or venous compression (Fig 2)

The swelling in the perineum is usually quite firm, tense, and usually moderately tender Both perineal periurethral abscesses and extravasations yield fluctuation with difficulty In extravasation the scrotum and penis are not tense, but pit on pressure and usually present no tenderness The thickness of the infiltrated scrotal wall precludes adequate palpation of the testes and epididymes The uninitiated frequently mistake the huge swelling of the scrotum to be the result of epididymitis There really should be no confusion, for in the latter condition, this organ is usually easily palpated and very tender When the epididymes are obscured by inflammatory hydrocele, the tenseness and lack of involvement of the scrotal wall are evident

In late cases there is enormous swelling of the scrotum and penis with edema, boggy, dusky redness, weeping and desquamation of the superficial layers of the skin Finally, irregular black patches of skin with occasional frank crepitation make their appearance Sir Benjamin Brodie² is quoted as remarking "In extravasation a black patch on the glans penis is a harbinger of death"

DIFFERENTIAL DIAGNOSIS

Urinary Extravasation

- 1 Rapid, progressive spread
- 2 Tendency toward symmetry
- 3 Poorly defined limits
- 4 Pits on pressure
- 5 Minimal tenderness except in perineum
- 6 Exploratory puncture may reveal any type of fluid in perineum, depending upon the cause
- 7 Marked toxicity with high incidence of jaundice

Periurethral Abscess

- 1 Slow enlargement and tendency to confinement
- 2 Tendency toward asymmetry
- 3 Well-marked limits
- 4 Induration and tenseness
- 5 Well-marked tenderness
- 6 Exploratory puncture reveals pus
- 7 Mild toxicity

Both conditions may coexist, and frequently extravasation begins as a periurethral abscess

Since both conditions require incision and drainage, the differential diagnosis is academic except for the urgency of diverting the urinary stream Moreover, some periurethral abscesses, associated with urinary retention, are best treated by the addition of an external urethrotomy or suprapubic cystotomy

TREATMENT

Operative intervention is essential, and always an emergency procedure Besides multiple incisions into the infiltrated tissues, diversion of the urinary stream is of paramount importance In various institutions, and at the Harlem Hospital, diversion of the urinary stream has been accomplished by one of three methods (1) Suprapubic cystotomy (2) External urethrotomy (3) Indwelling catheter

In the experience of the writer suprapubic cystotomy is most preferable because (1) it most effectually drains the bladder, (2) it reduces trauma during the acute infection to a minimum, (3) it puts the bulbocavernosus and external sphincter muscles completely at rest, (4) the tube is most easily cared for and kept patent, and (5) it is followed by perineal fistulae least often.

Perineal urethrotomy, to be correctly performed, requires the passage of a sound, or guide, upon which the urethra is incised. In a very toxic patient with a urethral canal already inflamed and obstructed, and possibly surrounded by abscess or thrombophlebitis, trauma and shock are added by the passage of an instrument. Thereby, thrombophlebitis, bacteremia, pyelonephritis,



FIG. 3.—Two views of a case of *chronic* extravasation of urine. Note the enormous edema of the penis and scrotum in the anterior view and the multiple fistulous openings as seen in the view from behind. (After Eisendrath and Rohnick.) This type of swelling probably results from either the presence of a perineal abscess of low virulence or chronic thrombophlebitis.

undue urethral hemorrhage, or rupture of the urethra may be induced. Frequently, patients with extravasation have not been circumcised. The prepuce is so edematous and infiltrated that it cannot be retracted to expose the external meatus. In this event urethral instrumentation cannot be accomplished until after a dorsal slit has been made. The latter requires either spinal or general anesthesia only to be followed by the problematic successful passage of urethral instruments.

This period unduly delays the operation, since one cannot foretell whether he will ultimately operate suprapubically, with the patient supine, or perineally, with the patient in the lithotomy position. This prolongation of anesthesia and manipulation is obviated by performing suprapubic cystotomy. In cases with extensive infiltration of the anterior abdominal wall it is conceivable that infection might be carried deeper into the fascial planes or space of Retzius by suprapubic cystotomy. Perineal urethrotomy with multiple incisions of the infiltrated tissues would be preferable in these cases.

External or perineal urethrotomy appears to be an easy and simple procedure, especially since another incision is not added to the perineal incisions necessary to drain the extravasation at this site. There is no doubt that the bladder can be effectually drained and the urinary stream diverted in this manner. However, as already indicated, (1) it requires unnecessary and

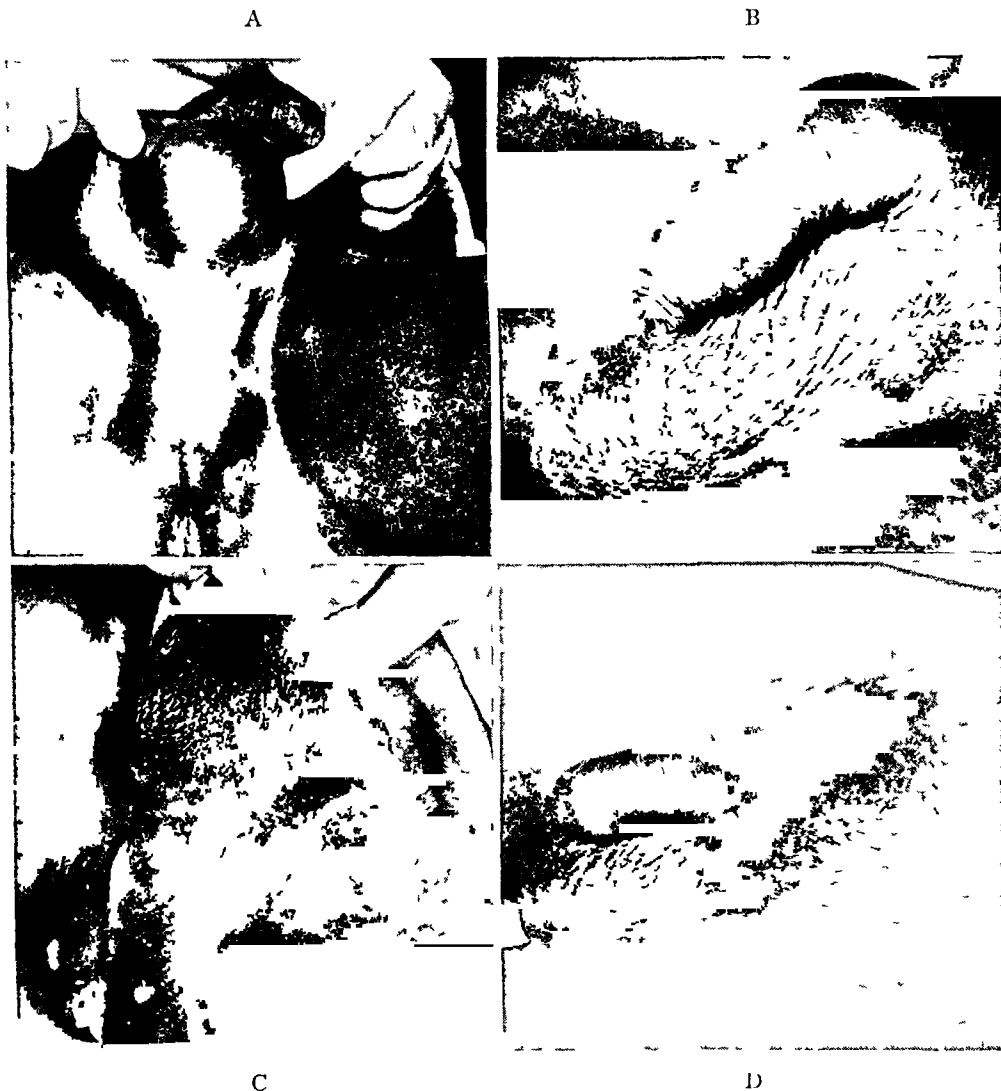


FIG 4—(A) and (B) are perineal and side views of a case of perineal abscess with edema of the dependent portion of the scrotum, the root of the penis and the left groin. Note the lack of continuity between the perineal and scrotal swellings, and the asymmetry of the scrotal and penile swellings. The two white scars represent drainage sites of preexisting ischioanal abscesses, unrelated to the perineal abscess. (C) and (D) are perineal and side views of the same patient one week after incision and drainage of the perineal abscess. The initial swelling of the scrotum, root of the penis, and groin disappeared three days after operation, without incising any of these edematous structures. The edema in this case, obviously, was due to the pressure of the abscess. This type of case is sometimes confused with actual extravasation in which the infiltrated tissues require incision.

harmful manipulation of the diseased urethra, (2) it does not so effectually put the urethral muscles at rest, (3) it is technically difficult with impassable strictures without a guide, (4) the tube is not so easily cared for post-operatively, and (5) it is followed more frequently by perineal fistulae. The defects resulting from the combination of disease (perineal abscess, stricture, and phlegmon) and the incision of the urethra are so great that they

make a very serious loss in the continuity of the canal. After the extravasation has been controlled, the patient stabilized, and the urethrotomy tube removed, a prolonged period of hospitalization is required by the manipulation and the use of indwelling urethral catheters in an attempt to heal the perineal fistula. Campbell¹ reports the necessity for five secondary suprapubic cystotomies as part of the plastic repair of these perineal fistulae.

Catheter drainage would seem feasible in those cases where the instrument could be easily passed into the bladder. But, as heretofore mentioned, those cases are the worst in which the patient persists in voiding and the canal is not completely obstructed either by disease or spasm of the sphincters. In a clean traumatic rupture of the urethra extravasation might be prevented by the use of an indwelling catheter, but once infection or extravasation has developed, the use of the catheter should be condemned. (1) In the presence of so much infection the catheter only aggravates the urethritis. (2) It is difficult to keep in place or patent. (3) It cannot be attached to the swollen and infiltrated penis. (4) It moves and loses the optimum site for drainage of the bladder, and urine is either retained in the bladder or forcibly expelled alongside the catheter—to aggravate the extravasation. (5) The presence of the catheter may induce prostatitis, seminal vesiculitis, epididymitis or thrombophlebitis. (6) It does not put the urethra at rest. (7) It results in the highest mortality.

We have seen cases of periurethral abscess incised and drained to be followed by extravasation in a day or two. Some members of the staff, unaware of the necessity for diversion of the urinary stream, have added secondary incisions and revisions to the progressively infiltrated areas, without improvement. But when the floor of the urethra spontaneously broke through creating a large perineal fistula, the patient immediately began to improve. Unfortunately, this mode of progress is not common when extravasation complicates periurethral perineal abscesses. But perineal fistulae do frequently follow these abscesses after incision or spontaneous rupture, thereby accounting for the ultimate improvement of the cases wherein multiple incisions are made without diverting the urinary stream.

TABLE IV
RESULTS OF OPERATIONS

Type of Procedure	Total Number of Cases	Number of Survivors	Number of Fatal Cases	Percentage Mortality	Hospital Days of Survivors
No operation	3	0	3	100%	
Suprapubic cystotomy with multiple incisions	11	7	4	36%	48.6
External urethrotomy, with multiple incisions	9	6	3	33%	56.3
Multiple incisions without operative diversion of the urinary stream	9	3*	6	67%	

* These 3 cases (Cases 14, 17 and 27) are discussed under PROGNOSIS.

Free incisions and drainage of the tissues involved in the extravasation are uniformly recommended by all writers. Experimental study has stressed

the importance of avoiding the tunica vaginalis testis. This pouch and the testicles are not involved, so that there is no necessity to incise and mutilate these structures. Although Campbell mentions the invasion of the tunica vaginalis testis in only one of his 135 cases, he and his associates continue to employ this procedure. The anatomic distribution of the fasciae, the roentgenographic demonstrations, and dissection of injected fluids, clinical experience, and autopsy records, combine to question the value of this procedure. Figure 5 shows the end-results of a patient treated by this method.



FIG 5—Showing the result in a case operated upon at another institution, where the scrotum was bisected, the testes bared and "swung free." Note the extensive scarring, the permanent retraction and elevation of the penis in a distorted position, the absence of the scrotum, the large perineal fistula with the remaining folds of scrotal and perineal skin held apart on either side, and the smaller urethral fistula more distally. The right testicle cannot be palpated. The left testicle is felt beneath the depigmented scar over the external inguinal ring, where it is fixed, tender and atrophied. The spermatic cords can not be felt, and the groins are occupied by long, continuous, adherent scars resembling those following herniotomy.

This patient was operated upon, April 5, 1938, at another institution, where he was confined until July 30, 1938. In spite of hospitalization for 16 weeks, the perineal fistulae remained open. He had been treated as an out patient until the time this photograph was made (August 9, 1939).

These results may be contrasted with Figure 6, which shows a patient treated by multiple incisions of perineum, scrotum, penis and groins and suprapubic cystotomy, without entering the tunica vaginalis testis.

In making multiple free incisions it is better to leave sufficient skin between the incisions by interrupting them frequently. The presence of small tunnels of skin does not prevent adequate drainage and it greatly facilitates healing. Long, continuous incisions are to be avoided.

The general condition of the patient requires strenuous measures. Continuous intravenous infusions of saline and glucose solutions, transfusions, administration of tetanus and anaerobic antitoxin and gas gangrene serum (although of questionable value), and sulfanilamide are advised.

Spinal anesthesia has given the lowest mortality in the Harlem Hospital series, but the series is too small to come to any definite conclusion.

Postoperatively, frequent wet dressings with warm solution of potassium permanganate, and later, hot sitz baths are used. Careful daily observation of the wounds is required to note whether further infiltration of tissue develops, so that prompt revision, secondary incisions or removal of sloughing tissue may be accomplished without delay. Following control of extravasation, subsidence of fever, and stabilization of the patient, gradual dilatation of urethral strictures is begun. This is most easily conducted while suprapubic drainage is continued. Periodic dilatation and careful follow-up will prevent recurrence.



FIG. 6—Showing the result obtained in a patient (Case 29) who had extensive extrusion involving the perineum, scrotum, penis, groins and supra-pubic region. All incisions were superficial with the exception of those entering the superficial pouch of Colles. The scrotum was not bisected, nor were the testes exposed.

No attempt was made to catheterize the patient since the penis was tremendously enlarged and edematous with early gangrene of the skin. The prepuce could not be retracted, so that a dorsal slit was made at the completion of the operation.

Under spinal anesthesia a supra-pubic cystotomy was first done through a clear field. Then the perineum was opened through paramedian incisions followed by multiple superficial incisions through the dartos layers of the scrotum and penis and through Scarpa's fascia of the groins and lower supra-pubic area. Copious amounts of 'pusious' fluid escaped from each incision, and the subcutaneous tissues appeared necrotic.

The patient was extremely ill and had a stormy course for a few days receiving tetanus and gas gangrene antitoxin, three transfusions, continuous intravenous infusions of glucose and saline solutions, sulfanilamide by mouth and frequently changed wet dressings of warm potassium permanganate solution.

The scarring of the perineum, scrotum and groins is so superficial that it is hardly discernible. The testes hang normally in a normal scrotal sac. The penis appears somewhat enlarged. Only a small redundant tag of the tremendously edematous prepuce remains following the circumcision performed three weeks prior to photography (August 9, 1939). The supra-pubic and perineal wounds are well healed and there is no urinary leakage from either wound. Prior to the removal of the supra-pubic Pezzar catheter the urethral canal was gradually and easily dilated to No. 30 F. Upon removal of the Pezzar catheter an indwelling urethral catheter was employed for a few days to facilitate closure of the supra-pubic sinus. The patient made a complete recovery with full restoration of his sexual power, without any disturbance in urination and without any mutilation.

PROGNOSIS

An analysis of 32 cases of extravasation at the Harlem Hospital forms the basis from which the following facts have been noted. Of the 32 cases collected from 1931 to 1939, inclusive, there were 16 deaths. The average

TABLL V
RESUMÉ OF 32 CASES OF URINARY EXTRAVASATION
Series from Harlem Hospital N. Y. C.

Case No	Days before Admission	Hos-pital Days before Operation	Days Onset to Operation	Type of Operation			Result	Days in Hos-pital	Comment
				Supra-pubic Cys-totomy	Ex-ternal Ureth-rotomy	No Op-erative Diver-sion			
1	10	0	10		+		Lived	33	
2	4	0	4		+		Died	15	
3	7	1/2	7 1/2		+		Died	3	
4	9	0	9		+		Lived	44	
5	10	0	10			+	Died	1	Multiple incisions only
6	7	1	8	+			Lived	52	
7	4	1	5			+	Died	2	Multiple incisions with cath-eter
8	2	13	15		+		Lived	44	Slow extravasation following urethrolithotomy
9	10	2	12			+	Died	11	Urethrotomy was unsuccessful
10	5	1	6			+	Died	2	Incision only
11	2	0	2		+		Lived	42	
12	2						Died	1	Moribund on admission. No operation
13	4	0	4			+	Lived	38	Condition limited to penis. Incisions and catheter
14	3	0	3			+	Lived	10	Multiple incisions only. Spontaneous perineal fistula
15	8						Died	1	Moribund on admission. No operation
16	5	0	5	+			Lived	73	Internal urethrotomy 1 mo before discharge
17	7	0	7	+			Died	2	Extensive extravasation
18	12	0	12				Died	7	Refused operation. Catheter only
19	3	0	3			+	Died	2	Multiple incisions only
20	4	1	5			+	Died	11	Multiple incisions only
21	3	4	7	+			Died	8	Delayed diversion caused death
22	3	0	3	+			Lived	33	
23	6	1 1/2	7 1/2	+			Died	3	Insufficiently wide liberating incisions
24	5	5	10	+			Died	5	Delayed diversion caused death
25	1	11	12		+		Died	15	Delayed operation caused death
26	2	2	4	+			Lived	71	
27	4	10	14			+	Lived	25	Probably only a periurethral abscess
28	7	1 1/2	8 1/2		+		Lived	79	
29	3	0	3	+			Lived	47	
30	4	6	12		+		Lived	96	
31	2	0	2	+			Lived	33	
32	21	1	22	+			Lived	31	Prolonged onset due to peri-urethral abscess with low virulence

A false impression may be derived from the average statistics of all cases without an intimate analysis. In some cases the process was unusually slow and prolonged because of low virulence and development from a periurethral abscess. This is illustrated by Case 32 in which 21 days elapsed before admission and by Case 8 wherein 13 days elapsed in the hospital before the extravasation was incised.

age of the survivors was 39 years, whereas the average age of the fatal cases was 50 years. Three principal factors contribute to the high mortality in extravasation: (1) Delayed treatment, (2) improper surgical management, and (3) severity of infection and toxemia.

Delay in treatment was occasioned both as a result of the ignorance of the patient and the errors of the physician. The circumstances which led to erroneous diagnoses merit emphasis. In many instances both patient and physician were unaware of an initial swelling in the perineum or of any disturbance in the urinary tract. The proportion of cases in which no complaint of pain or tenderness was recorded is remarkable. Another important factor which led to erroneous diagnosis and delay in diversion of the urinary stream, was that the patient continued to void. These factors led to an initial diagnosis of influenza, pneumonia, typhoid fever or brucellosis, with valuable loss of time and the performance of extensive laboratory tests, until the local signs were of such magnitude as to be unmistakable.

Of the 32 cases analyzed, 3 cases were not operated upon, and all 3 died. Of 11 cases subjected to suprapubic cystotomy, 7 survived, and of 9 cases subjected to external urethrotomy, 6 survived. Whereas in the 9 cases operated upon by multiple incisions, without any operative diversion of the urinary stream, only 3 survived. Of these latter 3 cases, which survived without operative diversion, the following explanation is offered. Case 13 presented a condition localized only to the penis and the urinary stream was partly, but inadequately, diverted by catheter. Case 14 developed a spontaneous perineal fistula after multiple incisions, thereby diverting the urinary stream and saving his life. Whereas Case 27 seemed to be only a localized periurethral abscess with thrombophlebitis.

Of the 13 survivors operated upon by suprapubic cystotomy or external urethrotomy, 9 were operated upon on the day of admission, whereas of the 16 cases who died, only 6 were operated upon on the day of admission. Of the 7 cases that died following suprapubic cystotomy or perineal urethrotomy, only 2 were operated upon on the day of admission, the other 5 cases presenting a delay of from one-half to 5 days before operation. Of the 7 cases (Cases 2, 3, 17, 21, 23, 24, and 25) that died following suprapubic cystotomy or external urethrotomy, the following number of days elapsed from onset to operation: 4, $7\frac{1}{2}$, 7, 7, $7\frac{1}{2}$, 11 and 12 days, respectively.

Jaundice appears to be one of the criteria in judging the severity of toxemia, besides the general condition of the patient and the blood chemistry data. Jaundice was present in 8 of the 32 cases. Of the 7 cases that died following suprapubic cystotomy or external urethrotomy, jaundice was present in 4. The 4 other cases with jaundice survived.

SUMMARY AND CONCLUSIONS

(1) A review of the clinical aspects of extravasation into the superficial perineal pouch is offered, with particular reference to the insidious cases and to the differential diagnosis from periurethral abscess.

(2) Emphasis is placed upon the emergency nature of the condition, and the necessity for early diversion of the urinary stream, besides multiple incisions of the infiltrated tissues

(3) Diversion is indicated irrespective of whether the patient is voiding well or not, and it is preferably accomplished by suprapubic cystotomy in the absence of abdominal involvement

(4) Avoidance of the deeper structures and the tunica vaginalis testis is stressed as a prevention of unnecessary mutilation

(5) Of 32 cases reviewed, 16 died. Of 3 cases not operated upon, all died. Of 11 cases subjected to suprapubic cystotomy, 7 survived, and of 9 cases subjected to external urethrotomy, 6 survived. Whereas, of the 9 cases operated upon, without any diversion, only 3 survived. Of the latter 3 cases, two had only localized conditions resembling perimeethial abscesses, and the other spontaneously ruptured his perineum, thereby adequately diverting the urinary stream and saving his life

(6) Of the last 7 consecutive cases treated in the latter part of 1938 and 1939, when the principles enunciated in this paper were emphasized, there were no deaths

(7) Three principal factors contribute to the high mortality in extravasation (a) Delayed treatment (b) Improper surgical management (c) Severity of infection and toxemia

REFERENCES

- ¹ Buck, Gudon, Jr. A New Feature in the Anatomical Structure of the Genito-Urinary Organs Not Hitherto Described. *Tr Am Med Assn*, 1, 367-372, 1848
- ² Brodie, Sir Benjamin. Quoted by Hamilton Bailey, *Physical Signs in Clinical Surgery*, 1930, p. 201
- ³ Campbell, M. F. *Surg, Gynec, and Obstet*, 48, 382-389, March, 1929
- ⁴ Colles, Abraham. A Treatise on Surgical Anatomy. Gilbert & Hodges, 1811, pp. 151-180
- ⁵ Finestone, E. O. *Surg, Gynec, and Obstet*, 73, No. 2, 218-227, August, 1941

EFFECT OF HEPARIN ON PHAGOCYTOSIS BY THE CELLS OF THE RETICULO-ENDOTHELIAL SYSTEM*

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IT IS NECESSARY TO STUDY the effect of heparin on certain of the fundamental processes that occur in the body. Phagocytosis by the cells of the reticulo-endothelial system is one of these processes. von Jansco,¹ in 1931, observed that the cells of the reticulo-endothelial system in the liver, spleen and bone marrow in rats and mice failed to take up colloidal gold during a period of ten minutes if heparin is given previously to the injection of the metal. Rigdon and Wilson² recently studied the effect of heparin† on capillary permeability and inflammation. It was shown in these experiments that staphylococci, when given intravenously to rabbits, localize and concentrate in areas of inflammation in the same manner in the animals given the heparin as in the controls. Furthermore, a colloidal dye, when given intravenously, localizes and concentrates in areas of inflammation in a similar manner in rabbits given heparin as in the controls. These two observations appear significant when one considers that both colloids and bacteria apparently localize and concentrate in an area of inflammation as the result of a change in the permeability of the endothelial cells in the small blood vessels.

Another observation made by Rigdon and Wilson² is that polymorphonuclear leukocytes apparently phagocytize staphylococci in the subcutaneous tissues of the rabbit in the presence of intravenously injected heparin in the same manner as they do in the subcutaneous tissues of an unheparinized rabbit. It may be possible that heparin has a different effect on the phagocytic activity of the fixed and the circulating cells, however, before such can be stated, additional experimental studies are indicated.

Wislocki,³ Lang,⁴ and others, have studied the fate of carbon particles injected into the circulation. These investigators find carbon particles in the Kupffer cells 30 minutes following the intravenous injection of a suspension of carbon. Intracellular carbon particles are present in the spleen 60 minutes following the injection. Lang⁴ states that "the 'endothelium,' or better, the histocytes, lining the sinusoids of the liver, the spleen and the bone marrow, accumulates large quantities of carbon particles immediately following the injection. In a majority of the capillaries and capillary veins the endothelium in the earliest stages shows various quantities of unevenly-sized carbon particles, single or in clusters, sticking to the free surface

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† The heparin is "Liquaemin", supplied by Roche-Organon, Inc

of the protoplasm" It is suggested by Lang⁴ that this phenomenon of phagocytosis is the result of the physical properties of the free surface of the endothelial protoplasm and it is due to a change in the surface tension of the latter

The present paper is a report of our observations upon phagocytosis of particles of india ink by the cells of the reticulo-endothelial system in normal rabbits and in rabbits given heparin preceding the injection of the ink

METHODS AND MATERIALS—Ten adult rabbits are used that weigh between 1.5 and 2.0 Kg. A five per cent saline suspension of Higgin's india ink is prepared immediately preceding the experiment in a quantity sufficient to inject all the animals. Five cubic centimeters of this suspension of carbon are injected into the marginal vein of the ear of five of these rabbits. They are killed 30 minutes later by a blow on the back of the head. Small pieces of tissue are removed from all the viscera and placed immediately in a 10 per cent solution of formaldehyde. The sections are prepared by the paraffin technic and are stained with hematoxylin and eosin.

Two cubic centimeters of heparin are injected into the marginal vein of the ear of five rabbits. Each of these rabbits is given intravenously 5 cc of the suspension of india ink five minutes following the injection of the heparin. Thirty minutes later these rabbits are also killed by a blow on the back of the head. Tissue is removed from the viscera and prepared for histologic examination.

Two rabbits are injected with 2 cc of heparin in a manner similar to those given heparin and india ink. Blood is removed from the heart 30 minutes later and 0.5 cc of it is placed into each of four test tubes (0.6x8.0 cm). The tubes are carefully inverted at frequent intervals to determine the time of clotting. Two normal rabbits are bled in a manner similar to those given the heparin and the blood is observed to determine the clotting time.

Experimental—Observations on the Clotting of Blood Following an Intravenous Injection of Heparin. The blood from the rabbits given heparin does not completely clot within 18 hours. In contrast to this the blood from the normal rabbits clots in five minutes. One of these two rabbits given the heparin died after approximately two hours. At autopsy, unclotted blood is present in the pericardial, thoracic and abdominal cavities. This hemorrhage apparently has its origin from the cardiac puncture. The second rabbit injected with the heparin is killed after two hours. Unclotted blood is present in the pericardial and the pleural cavities. It appears from these observations that the amount of heparin given to the rabbits is sufficient to demonstrate its effect on phagocytosis by the cells of the reticulo-endothelial system if it should occur.

EFFECT OF HEPARIN ON PHAGOCYTOSIS BY THE CELL OF THE RETICULO-ENDOTHELIAL SYSTEM

Sections from the liver, spleen, adrenal, gastro-intestinal tract, kidney, and lungs are studied microscopically. Carbon particles are present in the

spleen, the liver and the lungs in a larger quantity than in any of the other viscera. It is difficult to study phagocytosis in these sections of the spleen since there are such a large number of carbon particles, and, furthermore, it is difficult satisfactorily to identify each of the phagocytic cells in these sections. Carbon particles are present in the cytoplasm of the cells lining the sinuses of the spleen. They are present both free and in the cytoplasm of the large mononuclear cells in Billroth's cords. The white blood cells in the splenic sinuses have carbon particles within their cytoplasm. The greatest number of carbon particles in the spleen are located apparently in Billroth's cords. There is no difference as far as we can tell in the amount of carbon in the spleen of rabbits given heparin when compared with sections of spleen from the normal rabbits.

The liver is a much better organ than the spleen in which to study phagocytosis by the cells of the reticulo-endothelial system. The Kupffer cells frequently are filled with carbon particles. There appears to be a larger amount of carbon in the phagocytic cells in the walls of the hepatic sinuses surrounding the portal triads than in the cells in any other portion of the hepatic lobule. The cells lining the central veins only rarely contain any pigment. This variation in the degree of phagocytosis by the cells in different portions of the lobule may result from the anatomic location of the Kupffer cells and the point of entrance of the carbon into the hepatic lobule. There is no difference, however, as far as we can tell, in the degree of phagocytosis exhibited by the Kupffer cells in the liver of the rabbits given heparin before india ink and in the rabbits given only india ink.

A large number of the carbon particles are present in the interstitial tissue of the lungs. It appears that this is the primary site for the location of the particles. They are located, however, in the lumen of the small blood vessels in this tissue, and are either free or in the cytoplasm of the circulating leukocytes. Particles are found only rarely in the cytoplasm of any cells in the alveoli. There is no difference as far as we can determine in the number of carbon particles in the lungs of the rabbits given heparin and in the lungs of normal rabbits.

The sections of tissue from the organs other than the spleen, liver and lungs show essentially no carbon particles. There is, however, an occasional mass of carbon in either a glomerular tuft or in the cytoplasm of the cells lining a sinus in the adrenal. The leukocytes in the lumen of the blood vessels frequently have carbon particles within their cytoplasm. The greatest number of such cells are present in the lumen of the vessels in the spleen and the lungs. There is no variation in the amount of carbon present in the cytoplasm of the leukocytes and free within the lumen of blood vessels, in normal rabbits and those given heparin.

The endothelial cells lining the small blood vessels are carefully studied for the presence of carbon particles. There are no particles observed in these cells in either the group of rabbits given heparin or in the group of normal animals.

Discussion — Particles of carbon are present in the Kupffer cells and in the cytoplasm of the cells lining the sinuses of the spleen in normal rabbits 30 minutes following an intravenous injection of a saline suspension of Higgin's india ink. These findings are similar to those of McJenkin,⁵ Wislocki,³ and Nagao.⁶ We did not find any carbon particles in the cytoplasm of the endothelial cells in the small blood vessels.

There is no variation, as far as we can tell, in the amount of carbon in the sections from the group of rabbits given heparin and the controls. Apparently the quantity and the potency of this preparation of heparin is adequate, since the blood did not clot within a period of 18 hours.

Five cubic centimeters of a 5 per cent suspension of india ink is used in these experiments since this amount of ink is phagocytized by only a moderate number of the Kupffer cells within a period of 30 minutes. It is important to give only a small amount of ink in such an experiment, for the cells can phagocytize only a limited amount of materials within a specific interval.

The liver is the tissue of choice in the reticulo-endothelial system to study phagocytosis. Cells lining the sinusoids are the only ones that phagocytize carbon particles. These cells can be easily demonstrated in histologic studies. The spleen, in contrast to the liver, is a very unsatisfactory tissue for the study of phagocytosis of carbon particles. The quantity of ink is marked in the spleen, and, furthermore, the particles are present in both the sinuses and the pulp. It is difficult satisfactorily to identify each of the phagocytic cells.

A consideration of phagocytosis in the presence of heparin is important clinically. If this drug, in the quantity used in cases of thrombophlebitis, should be shown to inhibit phagocytosis of bacteria by either the circulating or the fixed tissue cells, there might be a definite contraindication for its use. The studies of Rigdon and Wilson,² and the present experimental observations, indicate that heparin does not inhibit phagocytosis, and as far as we know there are no contraindications to its use in cases of infected thrombophlebitis.

von Jansco¹ observes that 5–10 mg. of heparin when given intravenously to mice prevents the phagocytosis of colloidal particles of gold during an interval of ten minutes. When smaller doses of heparin are given phagocytosis is merely retarded. von Jansco¹ found that "Geimannin," a potent anticoagulant, does not prevent the precipitation and the phagocytosis of india ink. He did not study the effect of heparin on phagocytosis of india ink by the reticulo-endothelial system.

It is significant to observe the above variations of the two anticoagulants, heparin and "Geimannin," on phagocytosis. It is equally significant to recall that "the reticulo-endothelial elements, while possessing certain properties in common, are yet strictly selective and specialized in their activities in the various organs." The endothelial cells of the venous sinusoids are even more indifferent to particulate matter than to soluble dye.⁷

It may be concluded from the experimental studies already made upon heparin that it has no effect upon (1) The anaphylactic reactions,^{8, 9} (2)

capillary permeability¹, and (3) phagocytosis of staphylococci by polymorphonuclear leukocytes². The results of the present experiment may now be added to these observations, namely, heparin when given to rabbits in a quantity sufficient to prevent the clotting of blood for 18 hours has no effect, as far as we can tell, upon phagocytosis by the cells of the reticulo-endothelial system.

SUMMARY

There is no difference in the amount of carbon phagocytized by the cells of the reticulo-endothelial system in normal rabbits and those given 20 mg of heparin intravenously, when 5 cc of a 5 per cent saline solution of Higgins' india ink is injected intravenously five minutes following the heparin, and the animals are killed 30 minutes later. This amount of heparin apparently is sufficient to effect phagocytosis if such should occur since blood from rabbits given 20 mg of heparin does not clot completely within a period of 18 hours.

REFERENCES

- ¹ von Jansco, N. Pharmakologische Beeinflussung des Reticuloendothels. Klin Wochenschr, **10**, 537, 1931, Abst. Physiol Reviews, **16**, 383, 1931.
- ² Rigdon, R. H., and Wilson, Harwell. Capillary Permeability and Inflammation in Rabbits Given Heparin. Arch Surg, **43**, 64, 1941.
- ³ Wislocki, George B. The Fate of Carbon Particles Injected into the Circulation with Especial Reference to the Lungs. Am Jour Anat, **32**, 423, 1923.
- ⁴ Lang, F. J. Role of Endothelium in the Production of Polyblasts (Mononuclear Wandering Cells) in Inflammation. Arch Path, **1**, 41, 1926.
- ⁵ McJenkin, F. The Origin of the Phagocytic Mononuclear Cells of the Peripheral Blood. Am Jour Anat, **25**, 27, 1919.
- ⁶ Nagao, K. The Fate of India Ink Injected into the Blood. Jour Inf Dis, **27**, 527, 1920.
- ⁷ Cappell, D. F. Intravital and Supravital Staining. Jour Path and Bacteriol, **32**, 629, 1929.
- ⁸ Bradley, D., and Dragstedt, Carl M. Effect of Heparin on Acute Anaphylactic Shock. Proc Soc Exper Biol and Med, **31**, 532, 1934.
- ⁹ Reed, C. I., and Lawson, R. W. The Influence of Heparin on the Course of Anaphylaxis in the Guinea-pig. Jour Immunol, **13**, 433, 1927.

CARDIOCIRCULATORY DYNAMICS IN SURGICAL SHOCK¹

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IN THE STUDIES to be presented, physiologic observations are made on the circulatory status in man before and after a surgical operation. The changes in hemodynamics, respiratory gases, and various blood constituents are compared to the reported findings in secondary shock in humans.

Shock has proved itself to be such an intriguing and elusive problem that a large number of investigations have been carried out during the past 50 years. How much the understanding of the circulatory changes has been improved by these studies is illustrated by comparing the definition of shock given by Gross,¹ in 1872, with that given by Blalock,² in 1940. The earlier writer considered shock to be 'the manifestation of a rude unhinging of the machinery of life.' Blalock, on the other hand, after narrowing the problem down to hematogenic or secondary shock, states: "The initial and the most important alteration in the circulation is the diminution in the blood volume. This may be due to the loss of fluid which escapes from the body or into the tissues of the body, and there may be a local pooling of blood at the site of injury. The important distinguishing characteristic is that there is general vasoconstriction rather than general vasodilatation as in other types of shock. The decline in blood volume is followed by a decrease in the return of blood to the heart and hence in a decrease in the cardiac output. The development of hemoconcentration or dilution at this stage is dependent upon the relative losses of whole blood and of blood plasma, upon the presence or absence of dehydration and upon other factors. If the volume of the circulating blood continues to diminish, the blood pressure declines even though vasoconstriction is maintained. A continued depression of the blood volume and pressure results in a failure of the constrictor mechanism. All of these changes result in anoxia of the tissues, mainly stagnant in type. This is accompanied by general capillary dilatation, by an increase in capillary permeability, by a general loss of fluid, and by a multitude of other alterations."

While fairly general agreement concerning certain features of fully developed secondary shock has now been achieved, the same cannot be said of the earlier changes occurring before symptoms of shock develop. The relatively slow progress on this aspect of the subject appears in part to be due to

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the fact that satisfactory technics have not been available for use in humans. In the present studies methods have been employed which, we believe, are well suited to the elicitation in man of early changes trending in the direction of shock.

The development of a technic for catheterization of the right auricle in man³ provides a means of making direct observations on mixed venous blood as it returns from the tissues. Since simultaneous observations on arterial blood are readily available by arterial puncture, the net changes resulting from the passage of blood through the tissues can be noted. In addition, by simultaneous collection of expired air, the cardiac output can be determined by applying the Fick formula. Data on cardiac output and on the pressure in the right auricle and brachial artery provide information regarding cardiac dynamics. Furthermore, data on cardiac output and on the pressure, respiratory gas content, and other constituents of the blood entering and leaving the tissues provide information regarding the influences to which the peripheral blood is subjected. The material which follows represents the application of these technics to patients undergoing a surgical operation.

Choice of Surgical Operation—During a major surgical procedure several factors, including operative trauma, hemorrhage, other fluid loss, sedation and anesthesia, and nervous stimuli, all influence the resultant circulatory status.⁴ In order to compare the circulatory changes in a group of cases, therefore, it is desirable to have these influences comparable in each case. We attempted to obtain such conditions by standardizing the operative procedure and minimizing other factors. All cases underwent a first stage thoracoplasty, performed by the same surgeon. Blood loss was measured. Local anesthesia was used to avoid the systemic effects of general anesthesia,⁵ and small doses of sedatives were given as needed to prevent circulatory changes related to emotional stress.⁶

PROCEDURE—Patients to be studied were prepared for operation in the usual way, and received medication as listed in Table I. Before operation a ureteral catheter was introduced into the right auricle and cardiac output determinations made by ballistocardiographic and direct Fick methods, as described elsewhere.⁷ The thoracoplasty was then performed and cardiac output studies repeated postoperatively, without changing the position of the catheter. It remained in place for about two and one-half hours on an average. During this entire time a slow saline infusion was maintained through the catheter. Before, during, and after operation, frequent measurements of pulse rate, respiratory rate, arterial blood pressure, and auricular blood pressure were made. Arterial blood pressure was measured with the sphygmomanometer and auricular pressure with a saline manometer. Roentgenograms of the chest were taken in four cases at the end of operation, in order to relate the level of the tip of the catheter to the zero point on the manometer and thus facilitate correction of auricular pressure readings. In the other two cases, estimates were made based on fluoroscopy, previous roentgenograms, and actual chest measurements. The studies on blood and expired air which

1% and 0.5% procaine without adrenalin was used in all cases

TABLE I

							Operation			
Name	Age	Sex	Nativity	Ht in Cm	Wt in Kg	Body Surface Sq Meter	Disease	Procedure	Medication	Postoper Course
M M	33	F	Porto Rico	23 4	48 6	1 43	Pulm Tbc Cavity LUL	1st stage thoraco- plasty post Left R 1, 2, and 3 11 00-12 15 1st stage thoraco- plasty post Left R 1, 2 and 3 9 40-11 15 1st stage thoraco- plasty post Left R 1, 2 3 and 4 9 55-11 50	Numbutal 0 100 p o 7 30 A M Morphine 0 008 h 8 30 " Scopolamine 0 0003 h 8 30 " Morphine 0 010 1 v 11 05 " Pentothal 0 150 1 v 11 30 " Morphine 0 010 h 7 30 " Scopolamine 0 0004 h 7 30 " Numbutal 0 100 p o 9 00 " Morphine 0 010 1 v 9 00 " Sod amytal 0 200 p o 7 00 " Morphine 0 010 h 7 30 " Scopolamine 0 0004 h 7 30 " Morphine 0 010 1 v 10 00 " Pentothal 0 350 1 v 11 00 " Numbutal 0 100 p o 7 00 " Morphine 0 015 h 7 00 " Scopolamine 0 0004 h 7 00 " Morphine 0 010 1 v 10 35 "	Smooth

were required for cardiac output determination gave a complete picture of the respiratory gases in the blood and lungs. In addition pH measurements of the mixed venous and arterial blood were made with the glass electrode in two cases, providing the necessary information for finding the carbon dioxide tension and alkali reserve.⁸ At the time of each cardiac output study, additional arterial blood was taken for hematocrit and plasma protein determination. Blood loss during operation was estimated in one case by the weight of fluid lost from the operative site[†] and in the others by the amount of hemoglobin lost.[‡] The amount of saline given through the catheter was measured approximately.

RESULTS—The six patients studied were all "good risks," and none of them developed clinical evidence of secondary shock. The significant information describing the patients, the operative procedure, and postoperative course, are listed in Table I. The data on measurements made before and after operation are shown in Tables II, III, IV and V. The more important findings were

(1) *Cardiac Output*—Of the six patients studied, cardiac output determinations by the Fick method[‡] were satisfactory in four; the blood data being inadequate on J C, and the checks poor on J G. (The respiratory quotient [Table II] does not check with the ratio a/b [Table V]). Of the four satisfactory cases, two showed a slight increase in cardiac output after operation, and two showed a decrease.

(2) *Oxygen Intake and Oxygen Arteriovenous Difference*—J D and N S showed an increase in oxygen intake as well as in cardiac output after operation. As seen by reference to the Fick equation, the ratio of oxygen intake to cardiac output is equal to the oxygen arteriovenous difference. The arteriovenous difference, therefore, varies directly with the amount of oxygen removed from each unit volume of blood, and inversely with the volume-flow of blood per unit of oxygen used. An increase in arteriovenous difference, as shown by J D and N S, indicates a reduced volume-flow in proportion to the oxygen used by the tissues.

* In this case all surgical materials were weighed before operation and discarded when soiled with blood or plasma, into a known amount of water. After operation all the surgical materials and the water were again weighed, and the increase considered to be due to fluid lost from the operative site.

‡ The technic of Gatch and Little for determining hemoglobin loss was modified slightly. Blood-stained sponges were discarded into a known volume of normal saline, and hemoglobin determinations performed on this fluid by the Sahli or the oxygen capacity technic. Grams of hemoglobin lost were readily calculated and translated into terms of cubic centimeters of patient's blood.

$$\frac{1}{2} \text{ Cardiac output in L/min} = \frac{\text{O}_2 \text{ intake in cc/min}}{\text{O}_2 \text{ arteriovenous difference in cc/L blood}}$$

or

$$= \frac{\text{CO}_2 \text{ output in cc/min}}{\text{CO}_2 \text{ arteriovenous difference in cc/L blood}}$$

In the satisfactory cases these values checked fairly closely (Table V), and an average of the two values was used.

TABLE II

Name	Time of Study	Ventilation		CO Output† Cc /Min	O ₂ Intake† Cc /Min	Respiratory Quotient
		Rate	Liters/Min			
M M	Preop	20	6 39	139 5	175 5	793
	Postop	36	5 96	142 5	190 5	748
C DiL	Preop	18	5 17	131 0	172 0	762
	Postop	26	6 68	151 0	203 0	744
J D	Preop	22	7 62	181 0	234 0	775
	Postop	27	8 62	211 0	265 0	796
N S	Preop	14	6 34	190 0	182 0	1 045
	Postop	19	7 14	187 5	251 0	749
J G	Preop	14	7 06	205 0	263 0	781
	Postop	22	7 84	183 5	258 0	710
J C	Preop		8 47	227 0	305 0	746
	Postop		10 00	228 0	320 0	713

* Saturated gas at 37° C and prevailing barometric pressure

† Dry gas at 0° C and 760 Mm hemoglobin

M M and C DiL showed an increase in oxygen intake but a decrease in cardiac output after operation. On both accounts the arteriovenous oxygen difference increased, indicating, as before, that the volume-flow of blood in proportion to tissue needs was reduced.

(3) *Oxygen Saturation of Arterial Blood*—The oxygen saturation of the arterial blood was in all cases essentially unchanged after operation, regardless of changes in cardiac output, indicating that gas exchange in the lungs proceeded in a normal manner.

(4) *pH, Carbon Dioxide Tension, and Alkali Reserve*—In two cases the blood pH was measured, and with this additional information carbon dioxide tension and alkali reserve were determined. One of these cases showed an increased cardiac output after operation and the other a decrease. The blood of both cases was more acid after operation and showed increased carbon dioxide tension and reduced alkali reserve. In the patient whose cardiac output increased, the alkali reserve, although decreasing, remained within normal limits, while in the patient whose cardiac output dropped, the alkali reserve was definitely below the limits of normal.

(5) *Pulse Rate and Stroke-Volume*—The pulse rate changes bore no consistent relationship to minute-volume of cardiac output. Of the two patients whose cardiac output increased after operation, J D showed a marked increase in pulse rate, while N S showed very little, and of the two whose cardiac output decreased, M M showed a marked increase in pulse rate, while C DiL showed very little. The pulse thus gave no clue as to total cardiac output. Since the variations in absolute value of cardiac output were not large, stroke-volume varied inversely with the pulse rate in each case.

(6) *Auricular and Arterial Blood Pressure*—Patients whose cardiac output increased showed very slight reduction in auricular pressure and only small reduction in arterial pressure. Patients whose cardiac output decreased showed somewhat greater changes. Systolic pressure tended to drop more than diastolic.

(7) *Blood Loss and Saline Gain*—It so happened that the saline given approximated the volume of blood lost in all cases except M M. Her fluid

TABLE III

Mixed Venous Blood

Name	Time of Study	Carbon Dioxide				Oxygen*				Arterial Blood			
		Vol %		pH _s at 37° C		Cap Vol %		Sat %		pH _s at 37° C		Cap Vol %	
		Cont Vol %	Press Mm Hg	Cont Vol %	Press Mm Hg	Cont Vol %	Press Mm Hg	Cont Vol %	Press Mm Hg	Cont Vol %	Press Mm Hg	Cont Vol %	Press Mm Hg
M M	Preop	53.2		10.2		14.8		69.9		49.8		14.4	
	Postop	51.2		8.3		13.9		59.7		47.0		13.5	
C D L	Preop	51.9	42.4	7.41		17.2		72.2		49.2		16.2	
	Postop	50.0	49.4	7.31		16.1		62.1		46.3		15.2	
J D	Preop	49.9		13.8		19.4		71.1		46.2		18.2	
	Postop	45.6		11.9		17.3		66.9		41.7		16.7	
N S	Preop	58.1	49.0	7.36		16.9		72.2		54.3		15.8	
	Postop	55.5	50.9	7.30		15.5		60.6		51.9		14.1	
J G	Preop	55.9		13.2		17.8		74.1		53.3		16.7	
	Postop	53.6		10.3		16.2		63.6		50.8		15.2	
J C	Preop	52.5								46.9		19.2	
	Postop	46.9								42.1		17.6	

* Oxygen carried by hemoglobin not including that which is in physical solution

TABLE IV

Blood Pressure

Arterial

Plasma

Blood Loss

Name	Time of Study	Arterial			Hematocrit	Sp Gr	Protein Gm /100 cc	Cc	Method	Saline Infusion Cc
		Auricular Mm H O	Syst Mm Hg	Diast Mm Hg						
M M	Preop	39	110	88	35.8	1.0268	6.76	1200	Total fluid loss from operative site (weighing)	400
	Postop		90	70	32.9	1.0252	6.22			
C D L	Preop	55	120	65	38.9	1.0261	6.53	360	Hemoglobin loss from operative site (Sahlh)	400
	Postop	43	90	70	41.5	1.0248	6.09			
J D	Preop	57	120	80	48.8	1.0291	7.55	250	Hemoglobin loss from operative site (Sahlh)	100
	Postop	52	100	80	47.2	1.0288	7.45			
N S	Preop	120	118	86	42.8	1.0273	6.94	480	Hemoglobin loss (Sahlh)	700
	Postop	113	105	85	41.1	1.0266	6.70	620	Hemoglobin loss (O ₂ capacity)	
J G	Preop	68	140	90	41.8	1.0291	7.55	480	Hemoglobin loss from operative site (Sahlh)	400
	Postop	33	90	60	37.9	1.0278	7.11			
J C	Preop	37	100	70	46.8	1.0290	7.52	270	Hemoglobin loss from operative site (Sahlh)	100
	Postop	0	95	70	43.5	1.0271	6.97			

loss, as measured, exceeded the saline given by nearly 800 cc. There was a considerable drop in auricular and arterial pressures, a marked increase in pulse rate, and a drop in cardiac output in her case. In the other cases blood loss and saline gain could not be related to other measurements.

(8) *Hemodilution*—Dilution of hemoglobin was indicated by a drop in the oxyhemoglobin capacity of the arterial blood in every case.

Dilution of plasma was shown by a drop in plasma protein concentration in every case.

A reduction in the volume of cells relative to whole blood volume was demonstrated by a drop in hematocrit reading in five cases. The sixth case, C. D.L., showed an increase in the hematocrit after operation.

Discussion—The direct Fick method of cardiac output determination used in these studies is discussed elsewhere. Because of its theoretic soundness and because of internal checks within the method, it is thought to be the most reliable procedure available for the determination of cardiac output in humans. In addition, it is suitable for studies in which the patient's active cooperation cannot be obtained.

Previous studies comparing cardiac output determinations by the direct Fick method and the ballistocardiograph in normal man, showed that, under the conditions of those experiments and providing certain corrections were made, the ballistocardiograph was surprisingly accurate.⁷ It was, therefore, hoped that in the present studies the ballistocardiogram could be checked against the direct Fick measurements before and after surgery. Unfortunately, there were only two instances before and one after surgery in which the tracings were satisfactory. In general the ballistocardiograms could not be used for calculation of the stroke-volume, the form of the tracings being abnormal either because of too rapid pulse rate or because of extraneous vibrations.

Auricular pressures taken during operation showed a downward trend, as reflected in the pre- and postoperative figures. Moment-to-moment variations were slight, except in the case of M. M., who sighed and grunted a great deal. Sighing caused a sudden drop in auricular pressure and grunting a precipitous rise, presumably related to changes in intrapleural pressure. In five patients, the change of position from the back to the side caused an increase of about 50 Mm. of water in auricular pressure, regardless of which side was up, the sixth patient showed a drop of similar magnitude.

In the case of N. S. the recorded auricular pressures were about twice as high as in the other patients. Roentgenograms of the chest showed the tip of the catheter to be unusually low and anterior, raising the possibility that it might have reached the right ventricle.

The respiratory quotient for N. S. was abnormally high before operation. This is not readily explained since he was in a fasting state and was not markedly hyperventilating. His medication was comparable to that given the other patients and there was no reason to suspect a drug reaction. The excellent check which was obtained on blood gas analysis (Table V. Ratio

a/b) suggests that the high respiratory quotient represented the true state of the respiratory gases at that time

In the determination of blood loss from the operative site, the weighing method gave an estimate based on total fluid loss, including plasma, while the other method gave an estimate based solely on hemoglobin loss. The former would be expected to give somewhat higher results, but the large

TABLE V

Name	Time of Study	Pulse Rate	(a)	(b)	Ratio (a)/(b)	Cardiac	Cardiac	Cardiac Output	Stroke Vol	Cardiac Index
			CO	O		Output	Output			
			A -V	A -V		from	from			
			Diff	Diff		CO	O			
Cc /L	Cc /L	Data	Data	Av	Cc /	Sq Ml				
Blood	Blood	L /Min	L /Min	L /Min	Beat	B S				
M M	Preop	92	34	42	81	4 10	4 18	4 14	45 0	2 90
	Postop	124	42	52	81	3 39	3 66	3 53	28 5	2 47
C DiL	Preop	112	27	36	75	4 85	4 78	4 82	43 0	3 13
	Postop	116	37	52	71	4 08	3 91	4 00	34 5	2 60
J D	Preop	84	37	44	84	4 89	5 32	5 11	60 8	2 86
	Postop	130	39	48	81	5 41	5 52	5 47	42 1	3 06
N S	Preop	85	38	36	1 05	5 00	5 05	5 03	59 2	3 01
	Postop	95	36	47	77	5 21	5 34	5 28	55 6	3 16
J G	Preop	110	26	35	74	7 89	7 52	7 71	70 1	4 79
	Postop	94	28	19	57	6 55	5 26	5 91	62 1	3 67
J C	Preop	68						5 50*	80 9*	2 75*
	Postop	96						5 46*	56 9*	2 73*

* From ballistocardiogram

difference in calculated blood loss between M M and the other cases is thought to be only in part due to the difference in the technic of blood loss determination. None of the figures can be considered but a rough approximation.

The effects of sedation and anesthesia appeared comparable in all cases except one. M M, alone, showed signs of apprehension and moderate pain during operation, resulting in wide variations in auricular pressure and respiratory rate. These signs were not present before and after operation at the time when most of the measurements were made. The other patients ran a relatively steady course and gave no evidence of abnormal activity of the autonomic nervous system. All received a number of drugs in small doses as shown in Table I. While this, in itself, was undesirable, it was necessary to insure satisfactory anesthesia and a satisfactory subjective state.

The trends of the determinations made before and after surgery may be summarized as follows:

Regarding cardiac dynamics, the auricular pressure, or filling pressure of the right heart, showed significant diminution in the cases whose cardiac output declined after operation. Arterial pressure, invariably showed a slight to moderate drop. In relation to oxygen intake, cardiac output dropped in all cases.

Regarding the influences to which the blood was subjected in the tissues, the increased arteriovenous difference, increased carbon dioxide tension in the mixed venous blood, decreased alkali reserve, and decreased pH in im-

plied that there was slowing of blood flow relative to tissue metabolism, suggesting early peripheral stasis

An attempt to compare these observations with the findings in the literature on secondary shock in man, reveals that cardiac output, auricular pressure, and mixed venous blood studies have not been reported. Indirect evidence of reduced cardiac output includes the finding of reduced blood flow through the hand (Freeman, Shaw, and Snyder¹⁰), and the repeated clinical observation of collapsed veins, thready pulse, pallor of the skin and reduced surface temperature. In regard to auricular pressure, Fishbeig's¹¹ finding of a reduced peripheral venous pressure is suggestive. His figures of 10–20 Mm of water in shock cases are significantly lower than that of 37 Mm of water, found by Richards, *et al*¹² to be the average auricular pressure in normal man. Because of the necessary pressure gradient from the arm vein to the right auricle, it is implied that Fishbeig's cases of shock had low auricular pressures, that is, below 10–20 Mm of water. Indirect evidence regarding the mixed venous blood is provided by Freeman, Shaw and Snyder,¹⁰ who found the oxygen content of the peripheral venous blood markedly reduced in cases of shock. It is probable that the oxygen content of the mixed venous blood is likewise reduced in shock.

Reports of other measurements on secondary shock in humans are available for direct comparison with the findings presented. Arterial blood pressure,^{13–15} pH ,¹⁶ and alkali reserve¹⁶ have generally been found lowered, oxygen saturation of the arterial blood essentially unchanged,¹⁰ and pulse rate elevated.¹⁶ Hemodilution has been noted in association with hemorrhage,^{17, 18} but hemoconcentration is generally considered characteristic of secondary shock.¹⁹

In the literature on human shock, there are, in addition, references to many other types of study, among the more important of which are the determination of blood volumes,^{17–20} and the comparison of hemoglobin concentration in the capillary and venous blood.¹⁹ These procedures, unfortunately, were not included in the present investigation.

The changes noted after operation, in the cases studied, were, in general similar in direction but less marked in degree than those expected in shock. They represent physiologic alterations occurring in the absence of, but presumably related to, the shock syndrome.

The expansion of this type of study should lead to a better understanding of the progressive changes in shock, and, thus help to provide more acute diagnostic criteria and more effective therapeutic measures.

SUMMARY

(1) Studies of the cardiocirculatory status before, during, and after thoracoplasty performed under local anesthesia, were made on six patients. Four of the studies were technically satisfactory.

(2) The techniques employed included simultaneous collection of mixed venous blood, arterial blood and expired air; measurement of auricular and arterial blood pressure, and estimation of blood loss and saline gain.

(3) The various determinations derived from these technics showed the following trends. In relation to oxygen intake, cardiac output decreased, auricular pressure and arterial pressure showed a slight to moderate drop, arteriovenous difference and carbon dioxide tension in the mixed venous blood increased, and alkali reserve and pH decreased.

(4) The relationships of these findings to those expected in secondary shock are discussed.

REFERENCES

- ¹ Gross, S. D. *System of Surgery*. Philadelphia, H. C. Lea's Son & Co., 1872.
- ² Blalock, Alfred. *Principles of Surgical Care Shock and Other Problems*. St. Louis, C. V. Mosby Co., 1940.
- ³ Cournand, Andre, and Ranges, H. S. Catheterization of the Right Auricle in Man. *Proc. Soc. Exper. Biol. and Med.*, **46**, 462, 1941.
- ⁴ Moon, V. H. *Shock and Related Capillary Phenomena*. New York, Oxford University Press, 1938.
- ⁵ Snyder, J. C. The Cardiac Output and Oxygen Consumption of Nine Surgical Patients before and after Operation. *Jour. Clin. Investigation*, **17**, 571, 1938.
- ⁶ Freeman, N. E. Decrease in Blood Volume after Prolonged Hyperactivity of the Sympathetic Nervous System. *Am. Jour. Physiol.*, **103**, 185, 1933.
- ⁷ Cournand, Andre, Ranges, H. A., and Riley, R. L. Comparison of Results of the Normal Ballistocardiogram and a Direct Fick Method in Measuring the Cardiac Output in Man. *Jour. Clin. Investigation* (in press).
- ⁸ Peters, J. P., and Van Slyke, D. D. *Quantitative Clinical Chemistry Interpretations*. Baltimore, Williams and Wilkins Co., 1935.
- ⁹ Gatch, W. D., and Little, W. D. Amount of Blood Lost During Some of the More Common Operations. *J. A. M. A.*, **83**, 1075, 1924.
- ¹⁰ Freeman, N. E., Shaw, J. L., and Snyder, J. C. The Peripheral Blood Flow in Surgical Shock. *Jour. Clin. Investigation*, **15**, 651, 1936.
- ¹¹ Fishberg, A. M. *Heart Failure*. Philadelphia, Lea and Febiger, 1940.
- ¹² Richards, D. W., Cournand, Andre, Darling, R. C., and Gillespie, W. H. Pressure in Right Auricle of Man in Normal Subjects and in Patients with Congestive Heart Failure. *Trans. Assn. Am. Phys.*, 1941.
- ¹³ Cannon, W. B. *Traumatic Shock*. New York, Appleton and Co., 1923.
- ¹⁴ Cowell, E. M. Investigation of the Nature and Treatment of Wound Shock and Allied Conditions. IV. The Initiation of Wound Shock. Medical Research Committee, No. II, 99, 1917.
- ¹⁵ Fraser, John, and Cowell, E. M. Investigation of the Nature and Treatment of Wound Shock and Allied Conditions. I. A Clinical Study of the Blood in Wound Conditions. Medical Research Committee, No. II, 49, 1919.
- ¹⁶ Cannon, W. B. Investigation of the Nature and Treatment of Wound Shock and Allied Conditions. III. Acidosis in Cases of Shock, Hemorrhage, and Gas Infection. Medical Research Committee, No. II, 3, 1919.
- ¹⁷ Keith, N. M. Traumatic Toxemia as a Factor in Shock. VIII. Blood Volume in Wound Shock. Medical Research Committee, Series 26, 37, 1919.
- ¹⁸ Robertson, O. H., and Bock, A. V. Memorandum on Blood Volume after Hemorrhage. Medical Research Committee, No. VI, Series 25, 213, 1918.
- ¹⁹ Robertson, O. H. Memorandum on Blood Transfusion. Medical Research Committee, No. IV, Series 25, 143, 1918.
- ²⁰ Gregersen, M. I., Gibson, J. J., and Stead, E. A. Plasma Volume Determination with Dyes. Errors in Colorimetry, Use of the Blue Dye T-1824. *Am. Jour. Physiol.*, **113**, No. 1, 1935.

BRIEF COMMUNICATIONS

SPONTANEOUS RUPTURE OF A NORMAL HEPATIC DUCT

REPORT OF A CASE

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A REVIEW of the literature on the biliary tract fails to reveal the report of any case of spontaneous rupture of normal bile passages. The value of reporting the condition becomes even more apparent when one notes that records of hepatic duct rupture, even from obvious causes, are exceedingly rare.

The site of perforation in the biliary tract occurring from all causes in a group of 90 cases collected by McWilliams,¹ has been 91 per cent in the gallbladder, 4.4 per cent in the common duct, 3.3 per cent in the cystic duct, and 1.1 per cent in the hepatic duct. However, this latter case (Brunner²) was not of a spontaneous nature, but was due to the presence of one stone in the ampulla and two stones in the common duct. Fieland³ reported one of the earliest recorded cases of a ruptured hepatic duct. This was caused by a stone in this duct.

In 1829, Compagnac⁴ described the case of a man, age 35, who had received a violent blow upon the abdomen. He did not die until 18 days later, yet autopsy showed a rent in the left branch of the hepatic duct, and six pints of deep-green bile in the abdomen.

Other authors^{5, 6, 7, 8, 9} discuss rupture of the gallbladder, cystic and common ducts, but no mention is made of the possibility of hepatic duct rupture.

In this connection, the anatomy of the hepatic duct¹⁰ is worth reviewing very briefly. The two large biliary ducts, one from the left lobe and a larger one from the right lobe of the liver, unite just beyond the transverse fissure to form the hepatic duct. This duct is 20–40 Mm (three-quarters to one and one-half inches) long with a diameter of 4–6 Mm, descending one-quarter inch to the right and anterior to the portal vein in the lesser omentum to join the cystic duct in the formation of the common duct. The mucosa is of the columnar type and contains branched tubular gland-like structures.

Case Report—E. M., white, male, age 73, complained of severe abdominal pain of four days' duration, situated in the epigastric region and extending downward. The pain had been continuous. He had vomited at the onset and several times since. For the past few years, he had been suffering from gastric upsets and melena had been passed on several occasions. There was no history of trauma.

The patient denied all previous illnesses and claimed to have been in good health all his life. He stated that his habits had always been good. Family history was irrelevant.

Physical Examination—The patient was a well-developed and well-nourished white male, complaining of severe abdominal pain most marked at the pyloric region. Temperature 100.6° F, pulse 110, respirations 30. There was no cyanosis or jaundice. General examination was essentially negative other than for the abdominal findings. The

entire abdomen had a board-like rigidity, it was painful and tender, and resistant to palpation

Laboratory findings showed the urine to be negative. Hemoglobin 90 per cent, W B C 12,350, with 84 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes

Clinical Diagnosis—Perforated duodenal ulcer and peritonitis

Operation—Under ether anesthesia, the abdomen was opened through a five-inch, right rectus incision, beginning at the costochondral angle. Numerous adhesions were encountered, and free peritoneal fluid of a dirty yellow color was present. This had a slightly bloody appearance near the pyloric region. No perforation of the stomach or intestines or other organ was demonstrable, and because of the extremely poor condition of the patient no further manipulation or further exploration was deemed advisable. The peritoneum, fascia and skin were closed in layers, and a cigarette drain was inserted to the pylorus. The patient was very restless and perspired freely following the operation. He expired six hours later.

Autopsy—The right heart chambers were markedly dilated. The myocardium was of normal thickness and contained a fine, diffuse fibrosis throughout. The endocardium and valves were normal. The aorta and coronary arteries were involved by a moderate arteriosclerotic process. The lungs presented a slight passive congestion at both bases but were otherwise normal. The liver was small, lobulated externally, and was bathed in some 300 cc of thin, cloudy, odorless, yellow fluid. On section, it was markedly cirrhotic, and there was a considerable increase of fibrous tissue in the periportal spaces. The gallbladder was normal and contracted, containing no bile. There was a tiny perforation at the middle of the anterior surface of the hepatic duct, about 0.5 cm wide, through which could be expressed thin, golden bile. All the layers of the duct were of normal thickness and color, and the mucosa was smooth. No stones were found in the liver, biliary tract, peritoneal cavity or intestinal tract. The cystic and common ducts were normal. The cystic artery showed no thrombosis. The gastro-intestinal tract was free from perforations or other pathology, other than an acute engorgement of the serosa throughout. Several adhesions in the upper abdomen had been tied and severed. The spleen was soft and friable and of normal size. On section, the normal architecture was replaced by a soft pulpy substance. The pancreas was of normal size, shape, consistency and position, and revealed no abnormalities on section. The genito-urinary tract was essentially normal. Except for cirrhotic changes of the liver, microscopy was essentially negative. *Anatomic Diagnosis*—Spontaneous rupture of the hepatic duct, bile peritonitis, atrophic cirrhosis of the liver, coronary sclerosis, myocardial fibrosis, and acute cardiac dilatation.

CAUSES FOR RUPTURE—Four explanations for bile duct rupture have been advanced by Newbiger,¹² which are presented in modified form.

(1) *Increased Intraductal Pressure*, with bursting at the critical point of distention. This increased pressure is due to mechanical blockade by stones, reflex spasm of the sphincter of Oddi, or both. The critical point, in the cases described, is at the point of operation (*i.e.*, cystic duct stump, or at entrance of supraduodenal tube). Rolleston and McNee¹³ feel that in the case of a healthy gallbladder wall, it may be thinned from distention, and rupture may then take place from trauma, or as a result of sudden pressure brought to bear upon the gallbladder by contraction of the abdominal walls in violent straining, coughing, or in the vigorous abdominal contractions during labor.

(2) *Infection* (cholangitis) destroys the mucosa and elastic tissues, weakens the duct walls and lowers their resistance to possible intraductal pressure increases. Wolfson and Levine⁹ report three cases of spontaneous rupture of the common bile duct following choledochostomy. In two cases, the duct

contained calculi, while in the third, it was filled with a thick mucoid cast. In these cases, rupture occurred due to a subacute infectious process at the site of the choledochostomy. A similar case has been reported by Bernhard,¹⁴ except that the spontaneous rupture occurred three years after choledochotomy. Newburger¹² adds a case of his own and eight other collected instances.

(3) *Thrombosis* (possibly of the cystic artery) might account for cases in which the perforation occurs widely separated from an area of operative trauma.

(4) *Reflux of Activated Pancreatic Juice* through a common opening of the pancreatic duct and choledochus, with tissue digestion. The anatomic relationship between the common and pancreatic ducts also militates against such a possibility. In this situation fat necrosis should be present. Pure pancreatic juice will not produce fat necrosis unless activated by intestinal juice,²² and presumably by tissue kinases.

To the preceding explanations may be added five others.

(5) *Stones* overlooked at the time of operation may eventually produce a pressure necrosis of the wall. Although mention is made only of common or cystic duct stones, it is assumed that similar changes hold for hepatic duct stones. This is of greatest importance, since W. J. Mayo¹⁵ found that in almost one-third of the deaths following common duct operation for stones, autopsy revealed that all stones had not been removed. Others^{16, 17} have also found in necropsy material, large percentages of stones left postoperatively in the ducts. In perforations of the gallbladder, stones were associated in over 70 per cent of the cases. The point of extravasation may be microscopic. When the ulceration cannot be found on careful examination, Power,¹⁸ and Honnall¹⁹ feel it is strongly possible that a transudation of bile occurs. Power reported three cases of biliary peritonitis in which stones were found, but with the actual point of perforation overlooked. On the other hand, Walters and Snell²⁰ believe it remarkable that the mucosa of the common duct is changed so little in the majority of cases of stone in the common duct; the natural resistance of this epithelial surface to trauma seems to be high. Nevertheless, ulceration may occur at points where a stone becomes impacted. In spite of the dilatation of the common duct and inflammatory changes in its wall, rupture is rare.

(6) *Indirect Trauma* to the duct from external sources, such as falls, or auto accidents, may result in overstretching and tearing of diseased or even normal bile ducts. Although such cases have been reported occurring in the cystic and common ducts and gallbladder, they have not been mentioned in conjunction with the hepatic duct.

(7) *Direct Wounds* caused by saber, bayonet, and projectiles. Direct wounds may occur also accidentally during abdominal surgery²¹ or paracentesis.

(8) *Upward Traction* due to shrinkage of liver (cirrhosis of liver, or acute and subacute yellow atrophy) or the downward pull of the duodenum by adhesions may conceivably produce overstretching and tearing of the hepatic

duct Although these etiologic factors have not been mentioned in the literature, it is slightly possible that the cirrhosis and subsequent liver retraction, as in our case, might possibly result in a tear, especially if an element of trauma were also introduced Against this supposition is the chronicity of a cirrhotic process, and the compensatory changes in a gradual elongation of the duct, as well as the mobility of the duodenum In addition, no such case has been reported in the literature

(9) Finally, *carcinomatous invasion* of the duct may produce rupture, although other symptoms based on obstruction become evident very early

SUMMARY

A case of a spontaneous rupture of a normal hepatic duct is reported The causes for rupture of the biliary tract are considered A careful search through the literature failed to reveal a similar case

REFERENCES

- ¹ McWilliams, C A Acute Spontaneous Perforation of the Biliary System into the Free Peritoneal Cavity ANNALS OF SURGERY, 55, 235, 1912
- ² Brunner Quoted by McWilliams ¹
- ³ Freeland, J Rupture of the Hepatic Duct Lancet, 1, 731, May 6, 1882
- ⁴ Compaignac, J A J Quoted by S H Mentzer Bile Peritonitis Arch Surg, 29, 227, 1934
- ⁵ Lysaght, A C Traumatic Severance of Common Duct, Case Report Brit Jour Surg, 26, 646, January, 1939
- ⁶ Lewis, K M Traumatic Rupture of Bile Ducts ANNALS OF SURGERY, 108, 237, August, 1938
- ⁷ Edington, G H Traumatic Rupture of Bile Ducts, Drained, Cholefistulogastrostomy Brit Jour Surg, 20, 679, April, 1933
- ⁸ Long, L Traumatic Rupture Bile Duct South Med Jour, 22, 236, March, 1929
- ⁹ Wolfson, W L, and Levine, D R Spontaneous Rupture of the Common Bile Duct Surg, Gynec, and Obstet, 60, 747, 1935
- ¹⁰ Lyon, B V Nonsurgical Drainage of the Gall Tract Philadelphia, Lea and Febiger, 1923
- ¹¹ Jordan, H E A Text-Book of Histology 4th ed, New York, D Appleton and Co, p 422, 1927
- ¹² Newburger, B Spontaneous Postoperative Rupture of the Bile Ducts ANNALS OF SURGERY, 107, 558, April, 1938
- ¹³ Rolleston, H, and McNee, J W Diseases of the Liver, Gallbladder, and Bile Ducts 3d ed, London, Macmillan and Co, p 825, 1929
- ¹⁴ Bernhard, F Spontaneous Rupture of Choledochus Three Years after Choledochotomy Zentralbl f Chir, 64, 993, April 24, 1937
- ¹⁵ Mayo, W J Surgery of the Hepatic and Common Bile Ducts Lancet, 1, 1299, 1923
- ¹⁶ Bruening, A Statistisches uber 367 choledochotomie Deutsche med Wchnschr, 38, 1543, 1912
- ¹⁷ Demel, R Operative Behandlung der Steinerkrankung der Tiefen Gallenwege mit einem Bericht uber die Technik und Dauererfolge Klin Wchnschr, 15, 1649, 1936
- ¹⁸ Power, S Biliary Peritonitis Brit Med Jour, 2, 948, 1935
- ¹⁹ Horrall, O H Bile Chicago, U of Chicago Press, p 210, 1938
- ²⁰ Walters, W, and Snell, A M Diseases of Gallbladder and Bile Ducts Philadelphia, W B Saunders, 1940
- ²¹ Clute, H M Operative Procedures in Common and Hepatic Duct Injuries New England Jour Med, 206, 47, January 14, 1932
- ²² Kestner, O Virchows Arch f path Anat, 246, 305, 1923

COMMON DUCT OBSTRUCTION DUE TO PRIMARY CARCINOMA OF THE CYSTIC DUCT

RESECTION, WITH REESTABLISHMENT OF CONTINUITY OF THE COMMON BILE DUCT

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CARCINOMA of the cystic duct or of the common bile duct at the junction of the cystic duct is rarely amenable to surgical therapy. The patient here-with presented afforded an unusual opportunity to perform a successful radical operation. That the procedure was only palliative in this instance will be noted from the following report.

Case Report—Hosp No 459614. I A, male, age 57, was admitted to Mt Sinai Hospital, July 10, 1940, and discharged, September 3, 1940, with the history of having noted dark urine and light stools three weeks preceding admission. One and one-half weeks later, jaundice was noted with itching. There had been no other symptoms except a loss of six pounds in weight. The past history was essentially negative, except for a mild diabetes discovered four years previously, which was easily controlled by diet.

Physical Examination—The patient was a well-developed and well-nourished, deeply icteric male. The heart and lungs were normal. There was a large, smooth firm mass in the right upper quadrant of the abdomen extending down to near the umbilicus. This was apparently the liver. Blood pressure 126/80. **Clinical Diagnosis**—Carcinoma of the head of the pancreas, with common duct obstruction.

Laboratory Data—Hemoglobin 94 per cent, W B C 8,350, with a normal differential. Stools contained no bile, very faint trace of urobilin, and were free of occult blood. The prothrombin time was 80 per cent of normal. Urine: Faint trace of albumin, no sugar, concentrated up to 1,028 and had 2 to 3 plus bile, and urobilinogen 1-10. Blood Wassermann test negative. Blood urea nitrogen 12 mg per 100 cc, sugar 130 mg per 100 cc, cholesterol 300, and cholesterol ester 115. The icteric index was 81 and the bilirubin 7.0. The van den Bergh was direct, promptly positive.

Roentgenologic examination of the abdomen showed no evidence of radiopaque biliary calculus.

The patient was prepared for operation with intravenous vitamin K and bilon capsules by mouth. A citrate blood transfusion was administered on the day of operation.

Operation—Exploratory celiotomy was performed, July 16, 1940, under ethylene ether anesthesia. An upper right rectus incision disclosed adhesions among the omentum, liver edge, gallbladder and peritoneum, which had to be separated before further exploration could be performed. Both lobes of the liver were markedly enlarged, firm, but smooth. The gallbladder was large, tense, contained no stones, and yielded 150 cc of hazy, white fluid on aspiration, culture of which was negative. In the region of the common duct was an elongated, irregular firm mass with an adherent nodular mass, evidently a malignancy. The head of the pancreas was normal to palpation. The common bile duct was exposed above the neoplasm and found to be dilated. Aspiration of the duct in this area yielded clear faintly yellow-tinged fluid. The difference between the fluids in the common bile duct and in the gallbladder indicated that the obstructive lesion of the common bile duct was evidently blocking the cystic duct. Obviously, a cholecystogastrostomy was not indicated and it was decided to explore the lesion further.

This was done by skeletonizing the common bile duct and portal vein. A walnut-sized node was dissected away from the right lateral aspect of the vein near the duodenum (Fig 1). The gallbladder was then mobilized, the cystic vessels tied, and the cystic duct, which appeared to be involved by tumor, was mobilized to the common duct. The gallbladder was then used for traction and better exposure. It was then decided to perform a radical procedure and therefore, the common duct was severed about 1 cm above the entrance of the cystic duct and, also, at a point below, where it entered the pancreas under the posterior surface of the duodenum. The gallbladder, cystic duct, and 6 cm

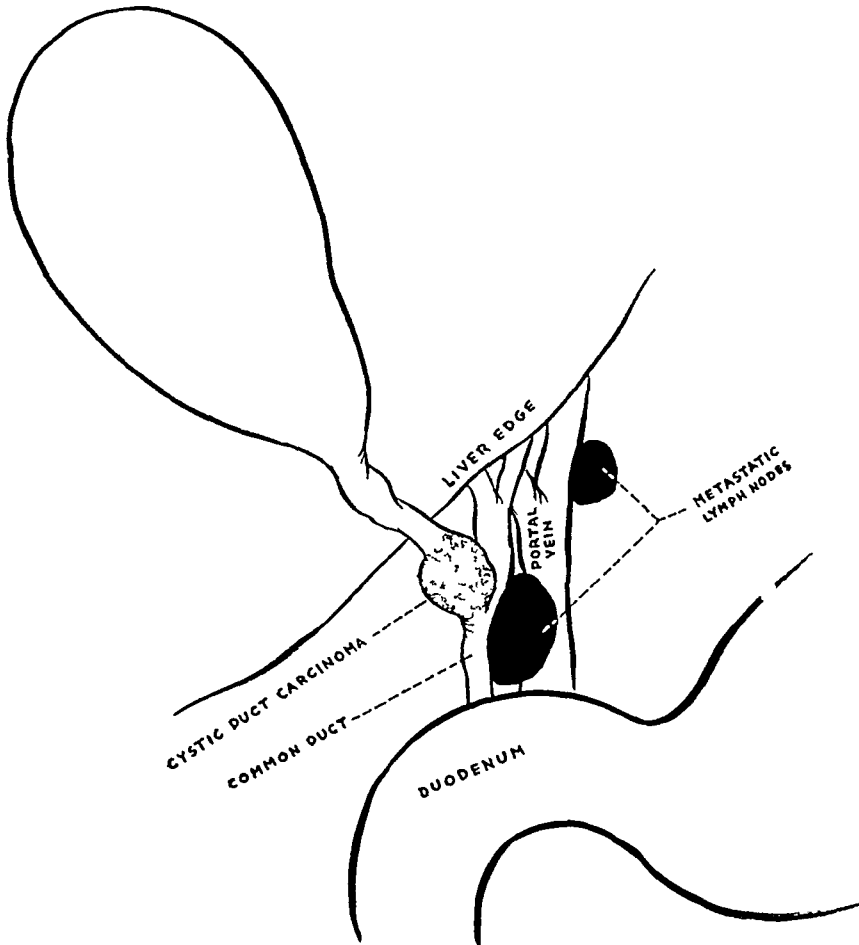


FIG 1—Diagram illustrating findings at operation

of the common bile duct were thus excised *en masse* (Fig 2). A pea-sized node, which was palpated on the superior mesial aspect of the portal vein, was then removed separately.

A medium caliber T-tube was used for reconstruction. The lower limb was placed for a distance of 1 cm into the distal stump of the common duct. A purse-string suture was placed around it through the pancreas and duodenum, with a suture through the tube and duct edge to keep it in place. The upper limb of the T-tube was placed into the proximal end of the duct, the cut edge of which reached to the vertical limb of the tube. Interrupted linen sutures were placed between the upper cut end of the duct and the duodenum, which brought the duodenum to it, folding the duodenum around the lower uncovered portion of the T-tube. Two large lappets of omentum were placed around the anastomosed area to further protect it. Iodoform gauze was inserted into the liver bed and a Penrose drain was placed down to Morrison's space. The wound was closed in layers.

CANCER OF CYSTIC DUCT

Subsequent Course—The convalescence was uneventful. The T-tube drained profusely and the jaundice became noticeably less as early as two days postoperative. The gauze and Penrose drain were removed on the sixth postoperative day, following which there was some slight, temporary biliary leakage around the tube. The patient was placed on vitamins and bile salts, he received several transfusions and rapidly regained his strength. On August 28, 1940, 43 days after operation, lipiodol was injected into the



FIG. 2.—Sketch of gallbladder, cystic duct with tumor and common bile duct which were removed at operation.

T-tube for purposes of making a roentgenologic examination (Fig. 3). This showed that the lipiodol flowed readily into the duodenum. The upper limb of the T-tube filled promptly and lipiodol passed into the hepatic radicles. The left major hepatic radicle appeared to be moderately dilated. There was perhaps slight dilatation of the right hepatic radicles. The common duct showed a moderate dilatation down to the tip of the lower limb of the tube. Beyond this point the duct was normal in caliber. The distal two inches of the pancreatic duct was filled with lipiodol by retrograde flow.

Following this procedure the tube was clamped off. There was no leakage and the stools were brown. The patient was discharged September 3, 1940, 49 days after operation.

Pathologic Examination—Dr. Paul Klemperer, Path. No. 71455. The specimen showed the presence of an adenocarcinoma of the cystic duct with lymph node metastases. The mucosa of the common bile duct was grossly uninvolved (Fig. 4).

Follow-Up—The patient showed a progressive improvement for seven months after operation. He gained in weight and strength and was well, except for a temporary peripheral neuritis of the legs and feet which responded to thiamin therapy. He also had pain in the left shoulder joint due to an arthritis, and roentgenologic examination of it and the spine showed no evidence of metastases. The T-tube was kept closed and undisturbed. There was never any leakage around the tube. His stools were normal and icterus did not reappear. However, after this time, he commenced to slowly deteriorate.



FIG 3.—Roentgenogram after injection of lipiodol into rubber T-tube. Note prompt flow into duodenum. Portion of pancreatic duct visualized.

At first, anorexia and occasional right upper quadrant abdominal pain appeared. Then weakness became marked, and he spent most of the time in bed. The liver enlarged and became hard and nodular, obviously the site of metastases. The patient became increasingly apathetic and died, June 8, 1941, about 11 months after operation. There was no postmortem examination.

COMMENT—Primary carcinoma of the extrahepatic bile ducts is, evidently, a rare condition, and carcinoma of the cystic duct is seldom seen at operation. In a recent exhaustive review, Stewart, Lieber, and Morgan¹ collected 27 cases, as instances of primary carcinoma of the cystic duct which were abstracted from the literature. These authors were unable to accept any of these cases, indisputably, as examples of cystic duct carcinoma. It must be remembered that most of these cases were postmortem studies, and, even if the tumor had arisen from the cystic duct, it was not sufficiently localized at

the time of examination to make its origin unquestionable. In the above reported case early operation revealed localization of the primary tumor to the lower end of the cystic duct. In spite of the short history, by the time the tumor had blocked the common duct by extrinsic pressure and angulation, causing jaundice, regional lymph node metastases had already occurred.

That carcinoma of the extrahepatic bile ducts can occasionally be treated by radical surgery is well worth emphasizing, and is the main reason for pre-

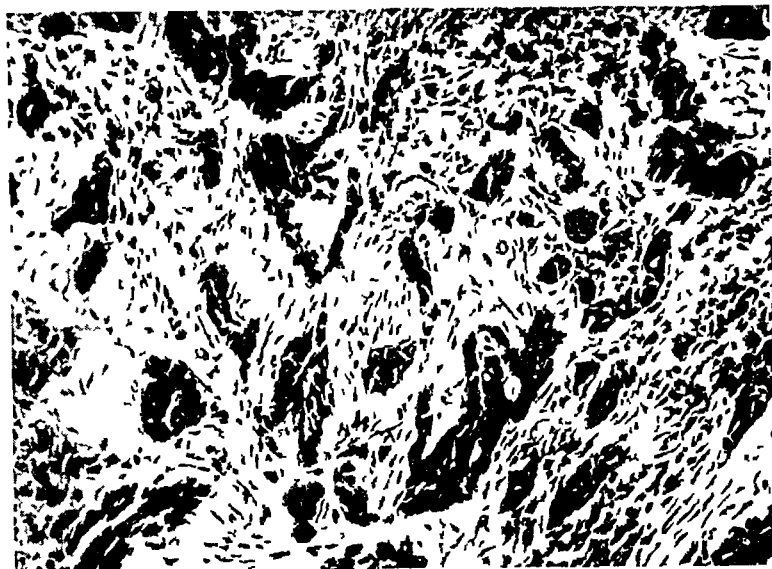


FIG. 4—Microscopic section of primary cystic duct infiltrating adenocarcinoma

senting this case. One of the most brilliant of the published cases is that of Garlock.² His case was that of a small primary carcinoma of the common bile duct at the entrance of the cystic duct. He was able to resect the gallbladder, cystic duct and a portion of the common duct, and then to perform an end-to-end suture of the common duct over a T-tube. This patient, although desperately ill at the time of operation, recovered and has remained well, without recurrence, for almost three years. A cursory review of the literature indicates that, occasionally, similar successful results have been obtained. Konjetzny,³ for example, presented a five-week result after radical resection of a common duct carcinoma. Amberger⁴ published a one and one-half-year result after resection of a common duct carcinoma, and mentions similar radically operated cases of Kehr and Doberauer. Renshaw⁵ found 20 cases of primary carcinoma of the bile ducts in the Mayo Clinic material during the years 1907 to 1921. In two of the cases of cystic duct carcinoma, stones were present in the gallbladder. One of the cystic duct cases was radically and successfully operated upon, with anastomosis of the common duct over a T-tube, and lived for three months.

Of particular interest in relation to the subsequent management of the rubber T-tube is a case reported by Moschcowitz,⁶ in 1912. While extirpating an acutely inflamed gallbladder with stones, he found a carcinoma of the common duct and resected it. A reconstruction was accomplished over a T-

tube, using the hepatoduodenal ligament and duodenum for covering the tube. However, he removed the T-tube on the twenty-fifth postoperative day, and a biliary fistula resulted. The case was presented before the New York Surgical Society at an early date, and the question was raised as to the necessity of performing a hepaticoduodenostomy. The T-tube in the present case was left severely alone. No untoward symptoms resulted, and it is evident that, unlike drainage tubes which are left in the urinary tract, encrustations do not form. Undoubtedly, the tube acted as a safety valve preventing obstruction from local recurrence and obviating stricture formation by scar tissue resulting from the defect in the common duct.

In summary, it may be stated that malignancies of the extrahepatic bile ducts should be treated by radical surgery when possible even in the presence of local lymph node metastases, since excellent palliative results have been occasionally reported.

REFERENCES

- ¹ Stewart, H. L., Lieber, M. M., and Morgan, D. R. Carcinoma of the Extrahepatic Bile Ducts. *Arch Surg*, 41, 662-713, September, 1940.
- ² Garlock, J. H. Primary Carcinoma of the Common Bile Duct. *ANNALS OF SURGERY*, 110, 474-477, September, 1939.
- ³ Konjetzny, G. E. Radikal Operiertes choledochuscarcinom. *Klin Wchnschr*, 5, 1349, 1926.
- ⁴ Amberger. Radikal Operiertes Carcinom des Ductus Choledochus. *Arch f Klin Chir*, 117, 189-192, 1921.
- ⁵ Renshaw, K. Malignant Neoplasms of the Extrahepatic Biliary Ducts. *ANNALS OF SURGERY*, 76, 205-221, August, 1922.
- ⁶ Moschcowitz, A. V. Resection of the Common Duct for Carcinoma. *ANNALS OF SURGERY*, 55, 610, April, 1912.

RECURRENT VOLVULUS OF THE SIGMOID COLON

AN UNUSUAL CASE REPORT

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ETIOLOGY—Although volvulus of the sigmoid colon accounts for less than 1 per cent of acute intestinal obstructions, its high mortality of 30 to 45 per cent makes it surgically important. It is rare in young people, and somewhat more common in males, presumably due to a stronger abdominal wall and smaller pelvis.

The most important factor in the etiology of volvulus is a long mesentery with a narrow attachment to the posterior abdominal wall. The anatomy of the sigmoid, therefore, renders it more susceptible to twisting than any other part of the intestinal tract. Inflammatory adhesions may increase the narrowing of the mesenteric attachment.

Chronic constipation is a contributing cause of volvulus. The precipitating factor may be insignificant, such as change of position, exertion, or a purgative.

Once the twist has occurred, distention of the sigmoid, and later of the bowel above, develops as a result of putrefactive processes together with the obstruction. If the twist is complete with circulatory disturbance, rapid changes in the loop take place.

Symptoms—In an actual acute attack, the chief symptoms are intermittent, colicky abdominal pain located near the obstruction, vomiting, constipation, and increasing distention of the abdomen. Tenderness and rigidity are rare. Temperature and pulse are normal. Peristalsis increases, and at times a mass may be felt in the left lower abdomen.

If unrelieved, the pain becomes more severe, but disappears with the onset of gangrene. Marked distention of the abdomen, tenderness and rigidity appear late, associated with necrosis of the bowel. In some instances the abdomen has a characteristic appearance, with distention at the sides and a groove in the center. Patients do not seem to become toxic as early with volvulus as with other types of acute intestinal obstruction.

Treatment—If volvulus is suspected or diagnosed roentgenologically, before the actual acute attack takes place, it is sometimes possible to abort it. The treatment of acute volvulus is entirely surgical. Purgatives and enemata are useless. When possible, an effort should be made to learn the state of the patient's hydration and general condition, during which time parenteral fluids may be administered and some of the distention relieved by Wangenstein suction siphonage or a Miller-Abbott tube.

To facilitate the operation itself, spinal anesthesia is best. Through a left

paramedian incision, the involved loop is located, is untwisted, and a long rectal tube inserted into it manually through the rectum, to allow the passage of gas and liquid feces. The loop may first be aspirated to facilitate untwisting. Unless gangrene is present, this is all that is required to relieve the immediate condition. The rectal tube is allowed to remain.

Procedures have been recommended to prevent recurrent attacks of volvulus. Plication of the mesentery and fixation of the sigmoid to the parietal peritoneum or side-to-side anastomosis between the two limbs of the sigmoid loop are usually unsuccessful. If gangrene is present and resection is not feasible, the segment may be brought out upon the abdominal wall and excluded, as in a Mikulicz procedure, perhaps with a cecostomy in addition. The consensus is that some type of resection of the sigmoid is the method of choice if the patient will tolerate the procedure. In some instances of recurring volvulus, relief may be obtained by a rectal tube¹ passed into the sigmoid under direct vision through a large sigmoidoscope.

Case Report—J. C., white, male, age 70, was first examined, March 14, 1934, following an attack of pain in the right lower quadrant. The diagnosis lay between acute intestinal obstruction and a right ureteral calculus, which had been passed. He was then well except for occasional slight pains and gradually increasing constipation until October 17, 1935, when he developed severe cramp-like abdominal pain and was unable to evacuate his bowels with laxatives, enemata, *etc.* He suffered with a distended abdomen, increasing pain, and nausea. He was admitted to the Delaware County Hospital, October 18, 1935.

Physical examination disclosed the abdomen to be markedly distended and tympanic, and peristalsis was hyperactive, with moderate tenderness in both lower quadrants. During the next 48 hours little success was obtained in deflating his abdomen with the use of the Wangenstein suction and colonic irrigations. Meanwhile, with parenteral fluids his general condition somewhat improved. A roentgenogram showed the sigmoid and ascending colon to be greatly dilated, and the sigmoid unusually long and tortuous. Gas was present in the small intestine.

Upon operation, October 21, 1935, a large distended loop of sigmoid was found filling the center of the abdominal cavity. The junction of the sigmoid and rectum was encased in adhesions, and the sigmoid was twisted on itself, causing a volvulus. The distal bowel was collapsed. After freeing the adhesions and relieving the volvulus, a rectal tube was passed into the sigmoid through the anus. Passage of a large quantity of gas and liquid feces relieved the distention. The patient's condition was so grave that the operation was concluded at this stage. His postoperative course was uneventful, and he was discharged November 11, 1935.

For the next year and one-half he remained well, and controlled his constipation with mineral oil. On April 2, 1937, he was again unable to evacuate his bowels for several days, developed abdominal pain and distention as before, and was readmitted to the hospital. When enemata and colonic irrigations proved ineffectual, the patient was placed in the knee-chest position, a large sigmoidoscope was inserted, and a rectal tube passed through it by direct vision into the sigmoid. A considerable quantity of gas was expelled. The rectal tube was left in position for 48 hours, at which time the patient's abdomen was flat, and he was discharged.

Since then he has had five similar episodes, each of which was relieved in a similar manner, without hospital admission. Numerous minor attacks of distention without pain have in the interim been relieved by the assumption of the knee-chest posture at home.

SUMMARY

This case is presented to illustrate that there are occasional instances where chronic volvulus may be relieved by a nonsurgical procedure, which has been reported previously¹. In desperate cases it can be considered as a substitute for operation or as a method of preparation of the patient until such time as he can stand surgical intervention. In our patient, relief has been so markedly effective that we have hesitated to recommend surgery in this case.

REFERENCE

- ¹ Hyman, Abraham. Recurrent Volvulus of the Sigmoid. *Am Jour Surg*, 4, 443-444, April, 1928.

MENINGOCELE SPINALIS TRAUMATICA SPURIA

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THE MOST FREQUENT complications in cases of fractures of the pelvis and the hip girdle are injuries to the kidneys, ureters, bladder, urethra and rectum. A particularly rare complication is injury to the spinal membranes, with passage of the cerebrospinal fluid into the soft tissues, which authors describe as "spurious posttraumatic meningeal hernia" *meningocele spinalis traumatica spuria*.

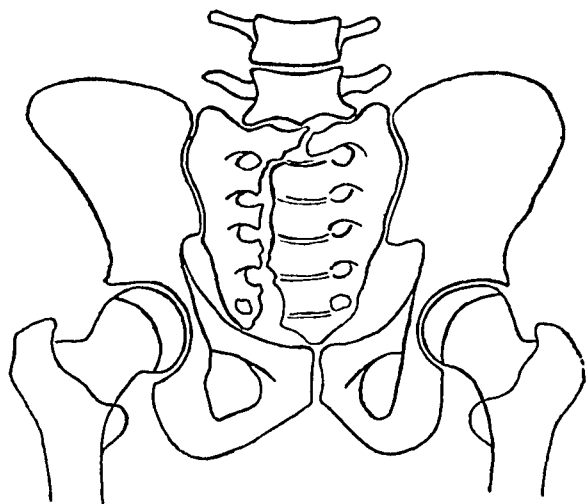


FIG. 1—Diagram of the fracture based on the roentgenogram. This diagram shows distinctly the line of fracture of the first sacral vertebra, consequently running along the sacral orifices.

We have found in the literature only two references to such cases, similar in many clinical details to the case observed by us. In both instances after trauma to the pelvis or the spine, the authors noted the appearance of a protuberance in the sacrolumbal region, containing a fluid which, after closer examination, was found to be identical with the cerebrospinal fluid.

In the case observed by Chodkow,¹ after a gunshot wound in the upper part of the spine, in a male, age 21, a paralysis of both lower extremities resulted, with loss of sensation to touch, retention of urine and feces, hematuria, and a protuberance in the sacro-iliac region. Compression of the tumor caused symptoms of increased intracranial pressure, such as headache, vertigo, nausea and bradycardia. In order to determine whether the liquid found in the tumor was connected with the subarachnoid space, a lumbar puncture was performed, and it was determined that the pressure was 125 Mm. Pressure exerted on the tumor caused a very marked increase of the pressure of the cerebrospinal fluid. Examination of the cerebrospinal fluid and of the fluid obtained from the tumor showed their identity both morphologically and chemically.

In the case reported by Schmidt,² a male, age 40, fell, and was injured in the coccygeal region. The roentgenogram showed a fracture of the fourth lumbar vertebra, and a tumor giving distinct signs of fluctuation was also

found. On the basis of these symptoms the author diagnosed an injury of the dura, with effusion of the cerebrospinal fluid through the laceration caused by the injury.

We shall describe our case somewhat more in detail, because of the rarity of this type of fracture and also because of the application of myelography in determining the site of injury of the meningeal sac and its communication with the spurious hernia.

Case Report—A male, age 26, fell from a tree, about ten meters high, striking the ground in a sitting posture, without losing consciousness after the accident.

He was taken home, where he remained three weeks without medical care and



FIG 2—Exposure immediately after an intrathecal injection of 2 cc of 40 per cent lipiodol, showing the passing of globules of lipiodol along the line of fracture of the sacral bone and gathering within the protuberance, descending into the intragluteal furrow.

without any therapy. He developed a severe headache, which continued for five weeks, although somewhat ameliorated.

After three weeks the patient tried to get up but could not stand on his feet. He did not notice any disturbance in urination, but complained, however, of constipation and pains during defecation, which he localized in the upper part of the rectum. The patient had a more severe headache when in the upright position, which he localized in the frontal region. He could not stand long. When standing, distinct fibrillations of the gluteal muscles, thigh, and the right leg could be seen. In attempting to walk he complained of pains in the right parasacral line. While walking he performed an adducting movement with the right extremity. The whole right limb showed muscular atrophy of a small degree, the right gluteal furrow was shallow, and somewhat lowered. The patient was able to maintain his equilibrium only by leaning on the right foot.

In the coccygeal region a protuberance could be seen, particularly on the right of the median line, about 13x11 cm in size, descending low into the intragluteal furrow. The skin over the protuberance was somewhat stretched but otherwise unaltered. In the area of the protuberance distinct ballottement could be determined. Examination by

rectum revealed an elastic protuberance on the posterior wall, and the finger entered between two oblong fragments of the sacral bone

Microscopic examination of the urine showed many white blood cells, phosphate crystals, and abundant bacteria. Spermatozoa were not found. Bacteriologic examination of the urine, both microscopic and on culture, showed *B. coli*.

FIG 3

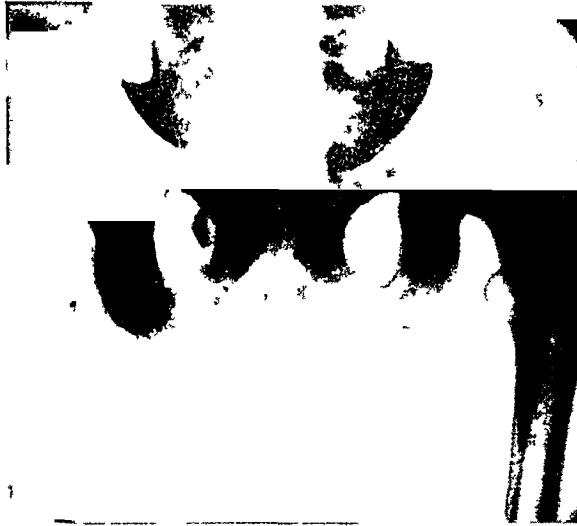


FIG 4

FIG 3—Exposure nine days after the intrathecal injection of lipiodol. The lipiodol has formed three larger globules in the lower part of the protuberance.

FIG 4—Profile exposure showing the lipiodol gathering at the level of the last coccygeal vertebra and also beneath it.

Neurologic Status—The cerebral nerves and the upper extremities showed no changes. The abdominal reflexes were, ambilaterally, present.

The lower extremities. The muscular tonus was, ambilaterally, normal. Adduction

of the right lower limb, both active and passive, was impossible because of pains in the region of the joint of the right hip. The motor power was normal. The knee and Achilles reflexes were present and equal. The muscles of the right thigh were sensitive to pressure, sensation was undisturbed, with the exception of a narrow band of hyperesthesia on the right buttock.

Chromocystoscopy showed no changes in the bladder, and no disturbances in the excretion of dyes.

Roentgenologic Examination—This revealed a longitudinal fracture of the sacral bone on the right side. Otherwise the bones of the pelvis showed no changes (Fig. 1). A lumbar puncture and a puncture of the protuberance were performed. Both fluids were somewhat xanthochromic. The fluid obtained from the protuberance contained somewhat more albumin, probably due to stasis. Otherwise the two fluids, both morphologically and chemically, were identical.

After an injection of 2 cc. of 40 per cent lipiodol, a roentgenogram was immediately taken. Roentgenograms were also made two and nine days later, in the anteroposterior and lateral planes. It can be distinctly seen on the roentgenograms how small globules of lipiodol pass through the line of fracture of the first sacral vertebra, and then along the anterior orifices of the sacrum, that is, along the line of fracture of the sacral bone, and gather to form a more or less solid mass within the protuberance descending into the intragluteal furrow (Fig. 2). After nine days, the lipiodol was noted forming four larger globules in the lower part of the protuberance, and a profile roentgenogram showed the gathering of the lipiodol at the level of the last coccygeal vertebra and also beneath it (Figs. 3 and 4).

At the time of severe headaches, the patient was given sedatives and also strong hypertonic solutions intravenously to counteract edema in the central nervous system. The patient's condition improved very rapidly. Eight weeks after the accident he was able to walk quite normally, and has no other complaints, other than the headaches, which recur paroxysmally. The protuberance in the lumbar region diminished slowly, the skin over the protuberance, previously extended, can be made into a crease. Being of the opinion that the aperture in the dura would close spontaneously, the patient, after spending five weeks at the Clinic, was sent home, and was told to return after three months, for a follow-up examination. At that time, five months after the accident, the protuberance in the sacrococcygeal region had disappeared entirely, and the patient had returned to his usual work as a farmer, complaining only of some sensations in the right parasacral region at the site of the fracture.

REFERENCES

- ¹ Chodkow. Meningocele Spinalis Traumatica Spuria. *Zentralbl. f. d. ges. Neurol. u. Psychiat.*, 43, 330, 1926.
- ² Schmidt. Über die Meningocele Spinalis Spuria Traumatica. *Jahresb. u. d. Leist. u. Fortsch. auf d. Geb. d. Neurol. u. Psychiat.*, 5, 673, 1901.

PERITONITIS DUE TO PERFORATION OF AN INFECTED URACHUS CYST

CASE REPORT

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FROM THE DIVISION OF SURGERY CLEVELAND CITY HOSPITAL CLEVELAND OHIO

Case Report—R B, colored, male, age 39, was admitted to City Hospital, January 23, 1940, complaining of abdominal pain of three days' duration. The patient had been in good health until the onset of the present illness. The pain began in the suprapubic region and gradually became generalized over the whole lower abdomen. It was a dull aching type of pain. There was a mild dysuria associated with the onset of pain. Twelve hours before admission he developed nausea and vomiting, and from that time on the pain seemed to be more severe in the right lower quadrant. This persisted until the time of admission. Past history revealed that he had developed a urethral discharge three months before, which was due to a balanitis. This cleared up with treatment. There was no other history of gastro-intestinal or genito-urinary disturbances.

Physical Examination—The patient was a well-developed and quite obese man, appearing acutely ill. Temperature 39°C, pulse 110, blood pressure 132/96. The abdomen was moderately distended. There was tenderness and muscle spasm over the whole lower abdomen, most marked in the right lower quadrant. There was marked rebound tenderness. No masses could be palpated. The genitalia were normal. Rectal examination showed marked tenderness of the pelvic peritoneum. White blood cell count 19,200, hemoglobin was 96 per cent. The urine showed albumin +, sugar +++++, acetone +++++, and a few pus cells. Blood sugar level 283 mg/100 cc, with a carbon dioxide combining power of 43 cc/100 cc. **Clinical Diagnosis** Diabetes mellitus, with acidosis and peritonitis, probably due to appendicitis. Diabetic therapy was instituted, parenteral fluids were administered and the patient expired four hours later.

Operation—Under spinal anesthesia, the peritoneal cavity was opened. Free pus was encountered. The appendix showed only a periappendical inflammation. A firm mass could be felt in the anterior abdominal wall, in the midline. It was extraperitoneal and just above the bladder. There was a perforation from the mass into the peritoneal cavity. In removing the mass, it was found to be firmly attached to the bladder, and to be attached to the umbilicus by a thin cord-like structure. The bladder was opened during this procedure, it was closed and the abdomen closed with drainage. The patient was quite sick for several days following operation, and the wound drained profusely. The diabetes was difficult to control during this time, but was easily controlled as the infectious process subsided. He was discharged on the nineteenth postoperative day.

Examination of the specimen showed acute and chronic inflammation, with sinus-tract formation. The cyst lining was almost completely destroyed by inflammation. No communication between the lumen of the cyst and the bladder could be found.

COMMENT—Although this is a rare condition nevertheless, it should be thought of in cases of peritonitis of obscure origin. In this case, the onset of pain in the suprapubic region and the accompanying dysuria gives a definite lead to the diagnosis. The physical signs which may have been present early were masked by the signs of peritonitis.

SPONTANEOUS AMPUTATION

ROBERT L SEWELL, M D

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ORDINARILY, the onset of a gangrenous process anywhere in the body will, of itself, cause a person to seek medical aid. There are, certainly, very few localities in this country so isolated as to prevent a patient from obtaining help, if only from neighbors. That a woman living and working in a large city should tolerate a gangrenous foot for six months until it fell off, through sloughing, is almost incredible. Such a case, however, has recently been seen by us.

While arteriosclerotic gangrene of the toes, the foot, and even of the entire leg is not unusual, the uninterrupted process going on to a spontaneous amputation at the ankle is quite rare in this country.

Case Report—R M H No 169826 K A, female, age 74, employed as a housemaid in an old apartment house. On September 21, 1940, she was brought to the emergency department of the University of Rochester Hospital by the police. A gangrenous foot covered with small maggots, and of vile odor, was also brought wrapped up in an old newspaper.

With some difficulty her story was finally pieced together. She had had no previous trouble with her extremities aside from an injury to the right foot 12 years before. At this time she had dropped a heavy box filled with metal on the external aspect of the ankle. She was lame for several weeks, but had no further difficulty until December, 1939. She then noted that the entire right foot below the ankle would get cold and numb, and was frequently discolored when she had been out in the cold. Through the succeeding winter months the foot assumed a purple hue and steadily became darker. It, apparently, caused but little pain, as she continued working and refused to become upset about the change. By April, six months before being brought to the hospital, the foot had become "just like leather" from the ankle down. While she was unable to bear weight on it due to some discomfort, and due to instability at the junction with the normal tissue, she continued at her work around the apartment house. She spurned canes and crutches and got around by supporting herself on the back of a chair. She frequently used the affected foot to balance herself.

About one week before entry, she noticed that the gangrenous foot had become much looser, and that there were some breaks in the skin around the edges. Moderate swelling of both legs below the knees developed. For the first time she began to notice a disagreeable odor and the presence of maggots about the lesion. The part rapidly became looser, until the day before admission when it fell entirely away from the stump except for "several strings in the skin and one 'leader' the size of a pencil." As it was then impossible for her to put on shoes and stockings and go about her work, she called the janitor of the building and had him sever the few remaining connections with his razor. She then applied hydrogen peroxide to the stump. This was the only medication ever used except for some "liniment" she had applied to the part sporadically. The police were notified by another tenant in the building and they brought her to the hospital where she was admitted despite her protests. She was rather indignant over the concern and interest which her condition elicited.

The past history revealed only the usual childhood diseases, moderate dyspnea on exertion for ten years, and nocturia for several years

Physical Examination showed an elderly woman with definite senile cerebral changes. She was thin, weak, very pale and very dirty. Scabetic lesions, maggots, and lice were

FIG 1



FIG 2

FIG 1—The granulating stump one week after admission. Note the ulcerated area on the anterior surface of the leg.
FIG 2—The gangrenous foot which was brought in with the patient.

thick on her body. The teeth were gone. The eye grounds showed retinal arteriosclerosis. The breasts were atrophic. There were many moist râles at the base of the right lung. The heart was slightly enlarged to the left and had an apical systolic murmur. The abdominal, pelvic and rectal examinations were normal. There were no glandular enlargements.

The stump of the right leg was for the most part covered by granulations. The ends of the tibia and fibula were partially eroded, but, as can be seen from the accompanying photograph (Fig 1), the articular surface of the tibia was, in places, still intact. The end of the fibula extended only to a point 2 cm above the end of the tibia. The granulations were quite redundant elsewhere, but of good color. There was a small, superficial, necrotic area in the skin 1 cm in diameter, which lay about 3 cm above the end of the stump.

Laboratory Data—The most significant was the anemia. On admission, the R B C 2.5 millions, W B C 7,800, hemoglobin 7.0 Gm. Urine showed only 2 W B C per high power field. She was given a small transfusion which brought her R B C to 2.8 millions, and a second one bringing it to 3.17 millions. She was also given iron by mouth. Blood proteins were a trifle low—the albumin being 2.94 and the globulin 2.82. Chlorides were 604 milli-equivalents. The fasting blood sugar was 135 mg per cent, and the glucose tolerance test was normal. Cholesterol was 163 mg per cent, and the CO₂ combining power was 47.

Her hospital course was relatively uneventful. Twenty days after admission a supracondylar amputation was performed under spinal anesthesia. This height was selected because the vessels below the knee were shown to be inadequate by oscillometry. She ran a moderate fever for the first three postoperative days, and had some increase in the basilar râles. She was given hyperventilation and a short course of sulfathiazole, and her resulting stay was uncomplicated. The stump healed by first intention. On her eighth postoperative day she was given instructions in crutch walking. She remained quite sullen, and would not cooperate in the least in learning to walk, so was transferred to a county institution on her tenth postoperative day.

On May 29, 1942, the patient was still alive and performing part of her original duties at the apartment house. She refused all further medical attention. She is able to get around with the use of one crutch.

A review of the literature brings to light very few similar cases, though they, too, are frequently as bizarre as this. One famous case was that of Rooke,¹ which occurred in a 14-year-old boy who had a fracture of both bones of the proximal portion of the forearm. While under observation, gangrene of the entire right arm up to the shoulder girdle developed. Sloughing at this joint eventually occurred spontaneously, with the formation of a satisfactory stump.

Often, in children, spontaneous amputation occurs after the onset of a "spontaneous gangrene." This, in turn, has usually followed an infectious process elsewhere in the body. Frequent forerunners of spontaneous gangrene are tuberculosis, diphtheria, less often scarlet fever and rheumatic fever. A careful analysis of these² has established the fact that the gangrene may be due to embolism, autochthonous thrombosis, or even to an endarteritis in which spasm of the vessels is prominent. Often several areas are similarly involved.

In adults, one of the chief causes of spontaneous amputation is thromboangitis obliterans, although usually only the phalanges are involved. However, several years ago we saw a middle-aged male with Buerger's disease with gangrene of the whole foot except for the heel. As there was no infection and no break in the skin surface he was followed conservatively in the hospital for five weeks until sloughing started. The process was then interrupted by removing the foot. This was accomplished very simply by cutting

through the joint capsule of the ankle and dissecting off the intact skin of the heel, and folding it anteriorly to cover the end of the stump. This end-result was entirely satisfactory. It is unwise, in Buerger's disease, to amputate the leg when the gangrene involves only the foot and not the heel.¹

Even more exceptional than in Buerger's disease is the occurrence of spontaneous amputation due to arteriosclerotic changes. While frequent losses of toes and fingers are cited, there is no previous report of a case in which a major spontaneous amputation has taken place, although this eventuality is frequently suggested.

The more customary, and far from unusual, course of events in arteriosclerotic disease is for amputation to be performed before actual sloughing of the gangrenous areas has started. Then, too, if spontaneous amputation is to occur, the demarcation must be right at a joint. Otherwise the bone will prevent loss of the part until it is eroded through by chronic infection.

The progression of such a case of arteriosclerotic gangrene could scarcely occur in a person with other than the peculiar phlegmatic make-up which this patient presented. Indeed it was only against her wishes that she was brought to the hospital after the foot was off.

Several factors evidently prevented the onset of acute difficulties earlier. Paramount, perhaps, was the fact that she maintained an intact skin surface up until the last several weeks. Otherwise the onset of an infection would have precipitated some action on her part, or would have called the attention of others to her earlier. Secondly, after the skin break occurred with inevitable infection plus the large amount of necrosis, it is likely that the maggots were beneficial in cleaning away the dead tissue connected to the granulating stump. Even when she first came into the hospital the granulations were healthy. A third significant factor in her case, which permitted the spontaneous amputation, or rather the disarticulation, to go on, was that the demarcation took place just at the junction of the astragalus with the tibia and fibula.

SUMMARY

A case of spontaneous amputation of the entire foot is cited in a 74-year-old woman. The underlying disease was arteriosclerosis, and the time necessary for the process was about six months.

REFERENCES

- ¹ Rooker. Spontaneous Amputation of Arm. *Am Pract (Louisville)*, 20, 210, 1879.
- ² Martin, W., and Shore, B. R. Juvenile Gangrene. *Trans Am Surg Assn*, 96, 415, 1928.
- ³ Samuels, S. S. Treatment of Gangrene Due to Thrombo-angitis Obliterans. *J A M A*, 96, 751, March 7, 1931.

SIPHON DRAINAGE FOR SUPRAPUBIC CYSTOSTOMY

O A NELSON, M D

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DURING the last 18 months we have used for patients with suprapubic cystostomy a siphon drain which has worked so well that rarely has the urine soiled the dressings. Consequently, excoriation of the skin and malodor from decomposing urine are prevented. Such a condition makes the convalescing period more pleasant for the patient, and attended by less suffering than when he is soaked in urine.

The use of the siphon also seems to promote healing of the incision, and to clear up the bladder infection much earlier than when the stagnated urine is allowed to remain in the bladder. Furthermore, nursing care and dressing expenses are very greatly reduced. In fact, the suprapubic incision is dressed only every day or two. In no instance have we seen irritation to the bladder, or any other harm, come from the use of this apparatus.

The employment of a siphon for bladder drainage is not new. It was described by Chiene,¹ in 1876, and by Boyd,² in 1936. During the last 25 years we also have tried to use a siphon drain with a fluid trap, but the drainage was not satisfactory until we splinted the part of the tubing forming the trap with a metal coil, and used a large catheter and large rubber tubing.

The apparatus consists of

- (1) A soft-bulb Pezzari Catheter Nos 30 F or 32 F (Baird, Inc, of New York make a catheter excellent for this purpose)
 - (2) A rubber tube seven feet long, of $\frac{3}{8}$ -inch diameter the wall of which should be $\frac{3}{32}$ -inch
 - (3) A metal coil at least six inches in diameter on the inside to go over the rubber tubing
 - (4) A large glass connection to connect the catheter to the rubber tubing
- The siphon is set up as follows

After the above articles are sterilized the Pezzari catheter is placed just



FIG 1—Siphon showing metal coil fixed in position on bed

inside the bladder. The rubber tubing is filled with sterile water, and all air expelled. The rubber tubing is connected to the catheter, and the metal coil passed over the distal end of the tubing. Then the coil is placed some inches below the bladder (preferable arrangement is to clamp it on the bedrail). Care must be taken not to place the coil too low, so as to cause too great suction, and pain to the patient. Care must also be exercised not to allow air to be sucked into the drainage system at the bladder or connection. It is well to tie both the catheter and the tubing on to the glass connection. If there is formation of urinary precipitate, the tube should be irrigated every day or two but mucus or pus does not clog the drainage system.

After suprapubic prostatectomy, we use the siphon as follows:

The suprapubic drain is left in place until the urine has been entirely clear for several days. Then a No. 22 F, three-eyed, open-end catheter is placed through the urethra, and the siphon system attached to the catheter. To hasten the healing of the suprapubic fistula, the bladder is distended once a day by injecting fluid through the catheter. After the bladder has been healed four or five days, the catheter is removed.

Practically all of these patients leave the hospital, with the suprapubic incision healed, in from 16 to 20 days after the enucleation of the gland.

REFERENCES

- ¹ Chiene, J. New Method of Wound Drainage. *Edinburgh Med Jour*, 22, 224-229, 1876.
- ² Boyd, Montague L. Suprapubic Cystotomy for Drainage. *Jour Urol*, 36, 740-755, December, 1936.

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AN INTRAPERICARDIAL TERATOMA AND A TUMOR OF THE HEART BOTH REMOVED OPERATIVELY

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I should like to report two lesions of the heart and pericardium. The patients presenting these lesions were referred to me by Dr Harold Feil to whom I am indebted because they form the basis of this report.

INTRAPERICARDIAL TERATOMA

Case 1—This patient was a white male, age 22. Complaints when admitted to the University Hospitals, June 25, 1934, were fever, weakness and pain in the chest. The patient had been well until February, 1932, when his symptoms first appeared. He was admitted to the Mt Sinai Hospital, Cleveland, in October, 1932. At that time the cardiopericardial silhouette was enormously enlarged (Fig 1), and 280 cc of bloody fluid were removed from the pericardial cavity by aspiration. The fluid was examined for tubercle bacilli but none were found. Signs of severe cardiac compression were present. Cardiac compression was relieved by the removal of fluid but recurred after each aspiration. The temperature fluctuated between 38° and 39.5° C. Improvement occurred during the month in the hospital but after one month at home he was readmitted because of the recurrence of symptoms. Aspiration (presumably of the pericardial cavity) yielded 500 cc of chocolate-colored fluid. A large, encapsulated, cyst-like outpouching of the pericardium appeared, with a smaller encapsulation just above it (Fig 2). The area of encapsulation was punctured by a needle but nothing was obtained. The patient had episodes of fever in 1933, but then improved and was at school during the first half of 1934. In June he developed fever again and was admitted to this hospital. The temperature was 38° to 39° C. The venous pressure in the arm was 14 cm of water. The arterial pressure was 110/70 mm mercury. Cyanosis, shortness of breath, palpitation of the heart and enlargement of the liver, which had been present intermittently in the past were not present when admitted to the hospital. Roentgenogram of the chest was about the same as in Figure 2. A slight precordial bulge was present to the right of the sternum.

First Operation—The fourth right costal cartilage was removed. A structure which was considered to be parietal pericardium was incised. It was 3 to 4 mm in thickness. This incision opened a cyst containing 300 cc of material which looked like water mixed with coagulated yolk of egg. The cyst was walled-off from the general pericardial cavity, which was not opened. At the base of the cyst the contour of the right auricle and the right ventricle was seen. The cyst was emptied and washed with solution of sodium chloride. The margin of the incision in the cyst was sutured to the pectoral muscle and the wound was loosely closed without drainage. Some

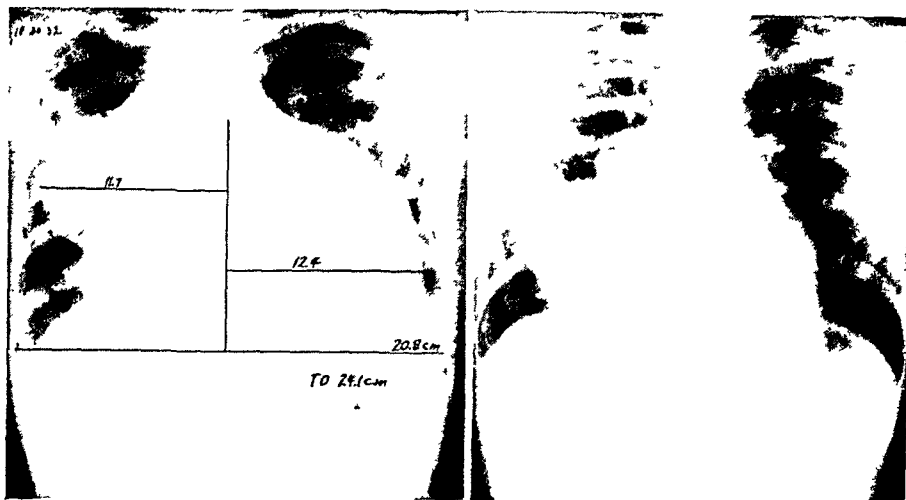


FIG 1 — Cardiopericardial silhouette is greatly enlarged. Bloody fluid was removed by aspiration. The heart was compressed (October, 1932)



FIG 2 — Roentgenogram taken January, 1933. Chocolate colored fluid, 500 cc removed by aspiration. Cyst like outpouching of pericardium, with a smaller mass just above it developed on the right side

FIG 3 — Lateral view of chest showing mass along right border of the heart (1936)



FIG 4 — A swelling appeared to the right of the sternum (March 1938)

FIG 5 — Roentgenogram March, 1938. The wall of the cyst shows deposition of calcium and some reduction in size

fluid seeped from the wound into the dressings for three days, but the wound healed and there was no further drainage. Examinations of smears of the material were reported to have shown bacteria but none were grown and guinea-pig inoculation did not show tuberculosis.

For the next two years the patient was improved, then his symptoms recurred. Doctor Feil reported that, in September, 1936, the venous pressure in the arm was 21 cm of water. Lateral view of the chest showed a mass extending along the right ventricle, right auricle and vena cava (Fig 3). This episode of cardiac compression was transient and he again improved until March, 1938, when he developed a swelling in the region of the operative scar (Fig 4). He was readmitted to the hospital. The temperature was normal. The venous pressure was 12 cm of water. No ascites. No enlargement of the liver. Roentgenogram of the chest is shown in Figure 5.

Second Operation—The scar of the original operation was excised and the mass was opened. Hair was found in the contents of the cyst. The cyst contained 350 cc of yellow fluid and masses of amorphous material. The cyst was emptied and its lining was washed with a solution of sodium chloride. In the base of the cyst the outline of aorta and pulmonary artery was seen. The wall of the cyst was then excised by sharp dissection. It was dissected from aorta, pulmonary artery, vena cava, right ventricle and right inferior pulmonary vein. It was densely adherent in the region of the great transverse sinus. At one time, while the dissection was carried out over the superior vena cava, the patient suddenly stopped breathing but started again after about one minute. Silver clips, ligatures and transfexion sutures were used for hemostasis. The cyst was completely removed (Fig 6). I had the impression that the wall of the cyst was fused with the parietal pericardium. Our artist's interpretation of anatomic relationships is shown in Figure 7. The wound was closed without drainage.

The patient was placed in an oxygen tent. Convalescence was uneventful and he was discharged from the hospital two weeks after operation.

Pathologic Examination—The cyst wall showed squamous epithelium, sebaceous glands, sweat glands and hair follicles. In some of the sections endometrium was found and epithelium resembling that of the upper and lower gastro-intestinal tract. Smooth muscle, normal fat and lymph follicles were also found. There was no evidence of malignant change. *Pathologic Diagnosis* Cystic teratoma. The appearance September, 1939, is shown in Figure 8. The patient has remained entirely well, four years after operation.

A thorough search of the literature on this subject has not been made. In 1933, Hedblom¹ reviewed the literature on intrathoracic dermoid cysts and teratomata, and referred to three instances of intrapericardial lesions. One additional case was found since this report was made. King² refers to a report by Somolinos³ which I have not obtained.

SYNOPSIS OF REPORTS OF FOUR INSTANCES OF INTRAPERICARDIAL LESIONS (*From the Literature*)

Reported by Ioŭl⁴. This patient was a boy, age 14. There was no clinical history. Necropsy examination showed a tumor, the size of a hen's egg, inside the pericardial cavity. The tumor had a smooth, glistening surface. It was attached to the pulmonary artery, aorta and the heart. It was densely adherent to the pulmonary artery and penetrated the wall of the artery into its lumen. The mass overlay the left coronary artery and the left atrium, and contained gelatinous material, fat, lymph nodes, smooth muscle, cartilage and calcium deposits. It was classified as a teratoma.

Reported by Mourat⁵. This patient was a male age 17. He was well until one year before death. The patient developed a mild fever, a cough and later on edema and ascites. The clinical diagnosis was tuberculous nodes in the mediastinum obstructing the superior and inferior vena cavae.

Necropsy examination showed an infected dermoid tumor in the mediastinum. The pericardial sac was greatly enlarged, but when this sac was opened it contained a large amount of pus from

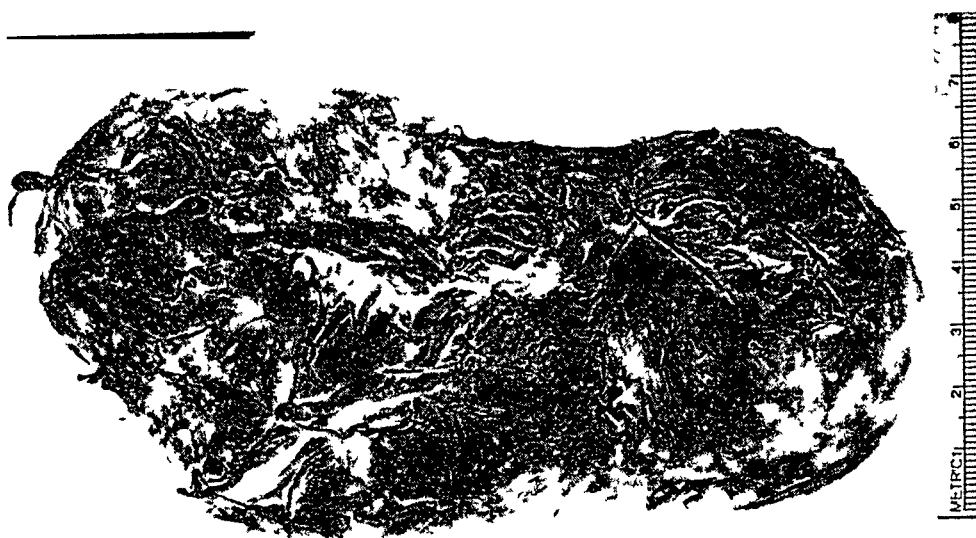


FIG 6 — Photograph of a teratoma removed from within the pericardium

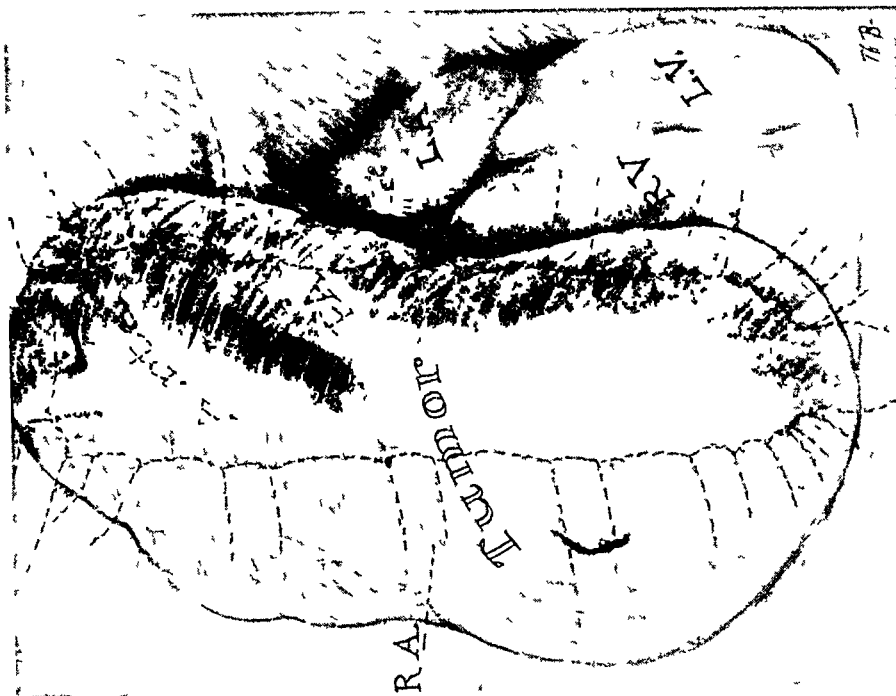


FIG 7 —Artist's interpretation of relationship between teratoma, right ventricle right auricle, aorta and venous cavity

TUMORS OF THE HEART

which streptococci were grown. It also contained yellow fatty masses and long hair. The heart was embedded in the thick posterior wall of the cyst, and there was no sign of any pericardial sac. The cyst appeared either to have grown from the pericardium or in its growth to have become very completely adherent to it.

Reported by Grimm⁶. The patient was a child, age three months. There was no clinical history except a provisional diagnosis of idiopathic hypertrophy of the heart. Roentgenograms showed an enormous shadow in the mediastinum. Necropsy examination showed a broad fluctuating tumor which filled the anterior aspect of the chest, both lungs being pushed posteriorly. The mass had a thin membrane as a wall, and appeared milky in color. Inside the mass a light colored lipid fluid was found. The heart was inside the mass and was of normal size, shape and position. There was an



FIG. 8.—Appearance one year after operation. Note the silver clips in the lateral view. The cardiac silhouette is normal.

intimate association between the adventitia of the great vessels and the mass. The tumor was lobulated with small orange sized growths of semicystic consistency. There were numerous perisized cystic compartments. On section, these were found to be multiloculated cysts with islets of homogenous tissue. In some of the cysts there was a semisolid material that looked like parboiled tapioca. In others a brain like substance was found. Bacteriologic study showed no growth. Microscopic examination showed glial cells, choroid plexus, skin, sebaceous glands, sweat glands, muscle, mucous glands, cartilage, intestinal tract and hair follicles. The pericardium was milk like in color but smooth and glistening. No evidence of malignancy. The author reported this case as one of intrapericardial teratoma. The relationship between the pericardium and wall of the cyst is not clear from the description.

Reported by Jellen and Fisher⁷. The patient was a white female, age three weeks. Cough and dyspnea were present since birth. When six days old the child had convulsions. During the second week attacks of cyanosis appeared. A presumptive diagnosis of idiopathic hypertrophy of the heart was made. An aspirating needle inserted into the mediastinal mass yielded nothing and a diagnosis of tumor was made. Necropsy examination showed a mediastinal mass within the pericardial sac. The pericardium over the mass was gray and thickened. When the pericardium was opened a tumor mass, 5 cm in diameter, was exposed. It was firmly adherent to parietal pericardium and to the wall of the right ventricle, to the right auricle, to the great vessels and the transverse aorta. It overlaid the bifurcation of the trachea. The pericardial sac contained 20 cc of clear yellowish fluid. The heart was not enlarged and was hanging from the mass as a small appendage. The mass was a multilocular cyst. Microscopic examination showed various types of epithelium, choroid plexus, smooth muscle, cartilage and glandular structures resembling pancreas. There was no evidence of malignancy.

Discussion.—It would appear that dermoid and teratomatous lesions situated within the parietal pericardium are of rare occurrence. The relationship between parietal pericardium and the wall of the cyst was not clear in any of the cases reported. It would appear that the parietal pericardium

may become an undistinguishable part of the wall of the cyst. These lesions can produce acute or chronic compression of the heart. They may become infected. Operative removal of the lesion was successfully accomplished in the case herewith reported. It would appear that operative removal is the only method of treatment.

TUMOR OF THE HEART, LEFT VENTRICULAR WALL

This patient was a white male, age 39, who complained of shortness of breath brought on by exertion, and a sense of constriction across the left side of the chest. He had been well until six years ago when these symptoms appeared. At first, the

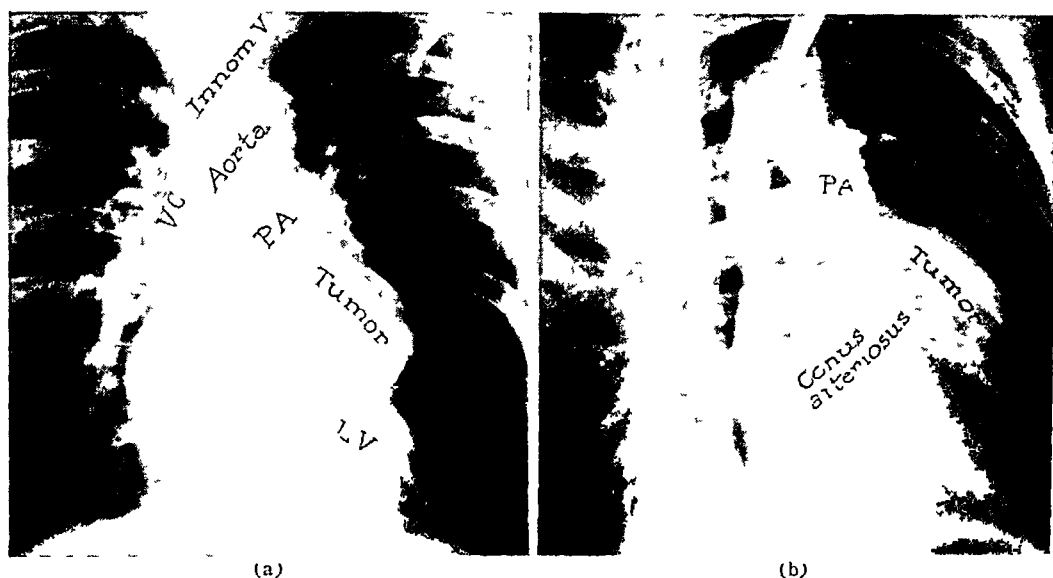


FIG 9—Roentgenograms of the heart. Diodrast was injected into a vein at the left elbow. (a) The innominate vein, the vena cava, and the pulmonary artery are shown. The tumor does not appear to communicate with any of the cardiac chambers. It is not an aneurysm. Calcification of the wall is present. (b) The right side of the heart wall is well visualized.

symptoms were mild but they increased in severity so that the patient had difficulty going to his office. These symptoms disappeared after he rested and they never came on while he was at rest, and suggested sclerosis of the coronary arteries as the probable cause.

The past history contained little of note. He had had typhoid fever from which he narrowly escaped death. There was no history of rheumatic fever, tuberculosis, diabetes or asthma. He had been quite active athletically as a youth, without any discomfort or any symptoms. The general physical examination, except the heart, was essentially negative. The skin over the face and neck showed scars of severe acne. An occasional extrasystole was noted. There were no cardiac murmurs. The arterial pressure was 120/72 mm mercury. The electrocardiogram showed slurring of the QRS complexes and slight left axis deviation. There were no additional changes brought out by exercise. Doctor Feil carries out fluoroscopic examination of the heart as a part of his routine examination. In this patient fluoroscopic examination led to the correct diagnosis. Special studies with diodrast were undertaken by Dr Eugene Freedman. Figure 9 shows the tumor in the heart. The left innominate vein, the vena cava, the right atrium, the right ventricle, the conus arteriosus, the pulmonary artery and the aorta can be identified. The tumor had a calcified wall. It did not fill with diodrast, and the pulsations of the lesion, as indicated by the kymograph film, were transmitted and were not expansile. The lesion, therefore, was not an aneurysm. I believed that we were dealing with a benign lesion of the heart—a tumor of some kind.

perhaps a dermoid. I also believed that this lesion produced the symptoms and, even though there was no precedent in the literature to support my attitude, I advocated operation.

Operation—September 7, 1940. The third and fourth left costal cartilages were removed. The pericardial cavity contained a somewhat increased quantity of clear slightly yellow fluid. The lesion in the heart was found. It was covered by epicardium. It could just be seen in our exposure (Fig. 10). Most of it was embedded in the myocardium but it did produce a bulge of about one or two centimeters from the general contour of the ventricle. An aspirating needle was introduced into it but nothing could be obtained. Two sutures were placed in the wall for traction and rotation. Considerable subepicardial fat was found around the base of the mass. This was dis-

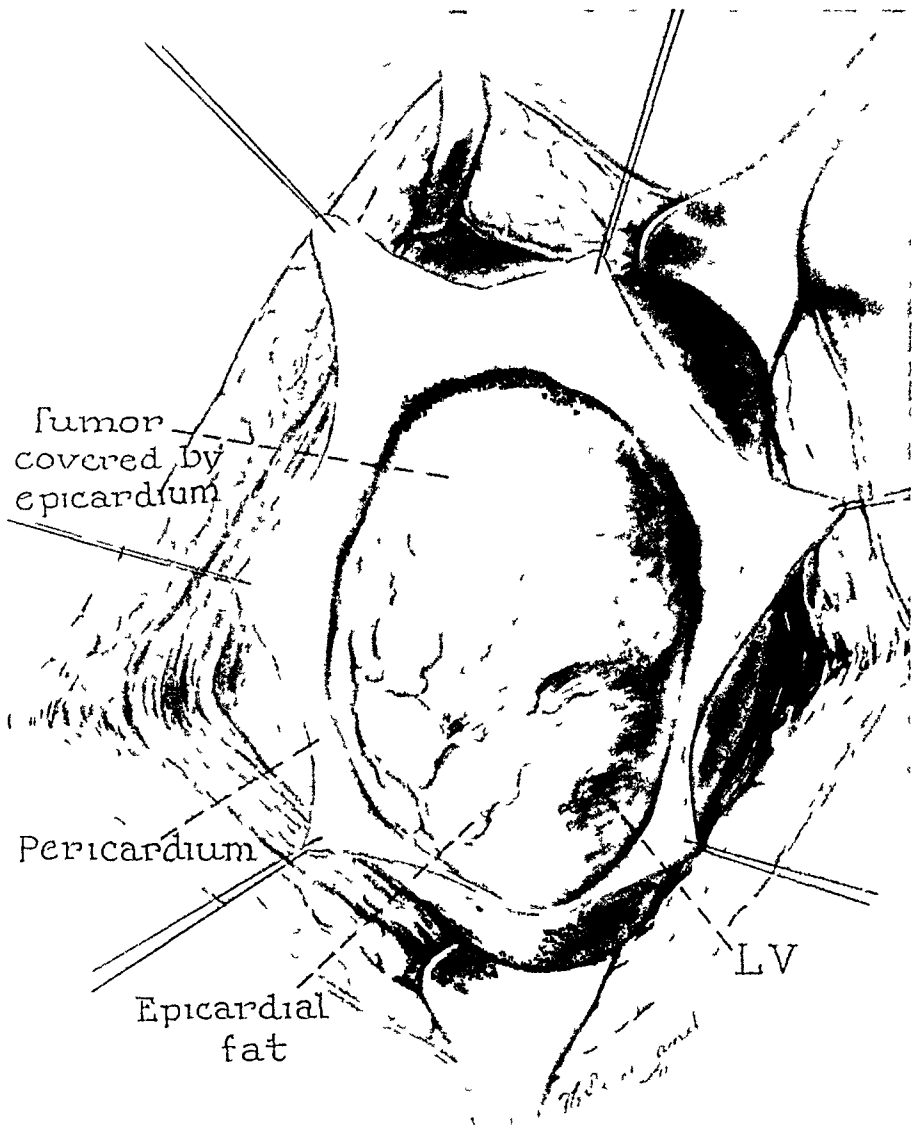


FIG. 10.—Appearance of the tumor after opening of the parietal pericardium.

sected from the wall. The descending ramus and the circumflex ramus of the left coronary artery were in this fat. A branch from the descending ramus penetrated the wall of the lesion. This artery was cut and ligated. I had the impression that these arteries were displaced by the lesion. Sharp dissection was used to separate the wall of the tumor from the heart muscle. The two tissues were sealed intimately together and blunt dissection, most probably, would have torn the myocardium. (It is sur-

prisingly easy to tear through the myocardium into the cavity of the heart) Sharp dissection was continued to the place shown in Figure 11. It appeared to be too much of a risk to continue further without knowing the nature of the tissues between the tumor and the cavity of the ventricle. The lesion was opened. The wall was calcified and was from one to three centimeters in thickness. The content was an amorphous material, homogeneous, with a consistency of packed clay. It was dark brown, and weighed 140 grams. This material was removed by curette and by washing with sodium chloride solution. There was no connection with the cavity of the heart nor could a weak area be found by palpation. The calcified wall was dissected from the

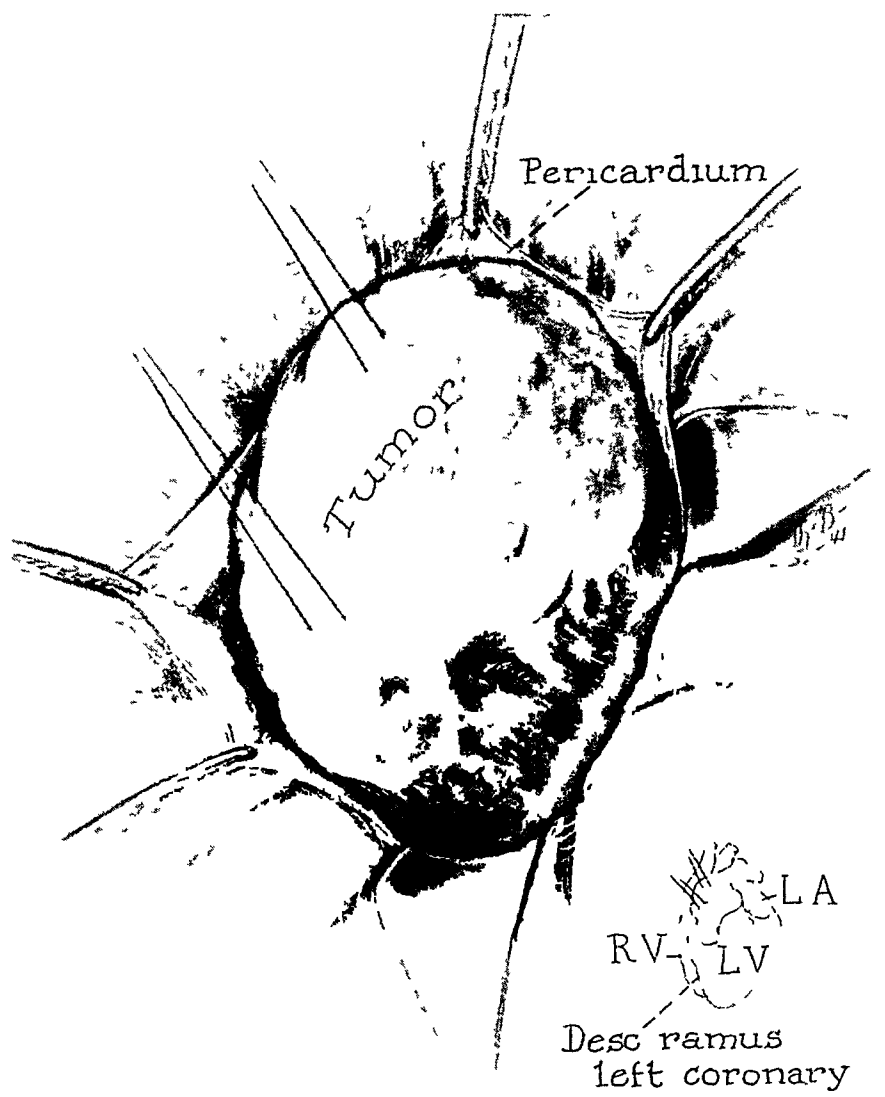


FIG. 11.—Subepicardial tumor of the left ventricle lying between the two branches of the left coronary artery. Traction sutures hold the tumor away from the myocardium. Sharp dissection was used up to this stage of the operation.

myocardium by sharp dissection. It was completely removed (Fig. 12). The bed consisted of cyanotic muscle. Digital palpation of the muscle was not carried out to determine how thick or how strong it was. The parietal pericardium was brought together by sutures. The wound was closed without drainage.

The patient made a satisfactory postoperative recovery. The electrocardiogram taken immediately after operation showed the T-wave in lead I to be inverted and

TUMORS OF THE HEART

S-T in leads 1, 2, and 3 to be slightly elevated. Six days after operation, ventricular extrasystoles were noted. These disappeared two days later. The pulse rate ranged from 100 to 130 for several days after operation. Over a period of one month it came down to about 90. The patient was discharged October 7, 1940. He was worried about his condition after he left the hospital. He frequently counted his pulse. He became stronger and found that he could make the trip to his office without shortness of breath. The feeling of constriction across the left chest disappeared. The electrocardiograms became entirely normal. The patient appears to be cured.

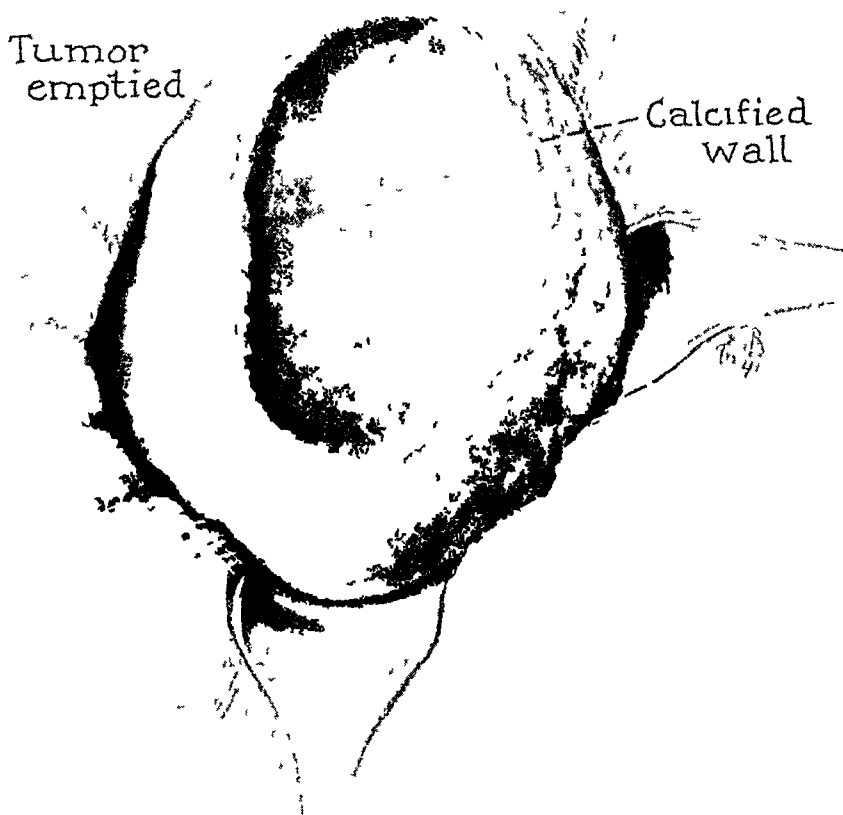


FIG. 12.—The wall of the tumor is incised. It was calcified. The contents were removed by curette. Complete dissection was then carried out successfully.

Pathologic Examination—Dr. Howard Karsner: "The wall of the cyst shows nothing indicative of true neoplasm. It is simply a capsule of connective tissue, the interior aspect of which is necrotic and calcified. Chemical examination of the cheesy content of the cyst showed no iron. The lipid content determined on a specimen dried to constant weight and weighing 4.41 grams was as follows: Total fat 13.25 per cent, cholesterol 6.45 per cent. It was estimated that the same quantity of dried whole blood would contain total fat 3.59 per cent, cholesterol 0.81 per cent. The chemical examination gives no specific information because as far as can be learned there is nothing known of the composition of a hematoma after it has been present a long time."

COMMENT—Before operation I thought this tumor might be a dermoid.

but we found no hair or other recognizable tissue in its contents. It had a calcified wall which did not show any epithelium or foam cells. It was not a xanthoma. The contents of the lesion had the consistency of packed clay, and between the gloved fingers it felt greasy. We cannot classify the lesion except to say that it does not appear to be a true neoplasm.

The question comes up as to whether an aneurysm will develop at the site of this lesion. I have carried out experiments for the purpose of producing aneurysms of the left ventricle. In these experiments a sphere of metal was introduced into the left ventricle by way of the auricle. The metal ball



FIG 13—These roentgenograms appear to be normal, 18 months after operation

was held firmly in position and pressure was applied to it through the myocardium. The myocardium could be crushed in this way between finger and metal. The metal could be seen through endocardium and epicardium. An aneurysm did not develop in these experiments. In other experiments the myocardium was sliced away, and in these experiments the parietal pericardium grafted itself upon the wound and an aneurysm did not develop. In this patient I should expect the parietal pericardium to become adherent to the myocardium at the site of the lesion and I should not expect an aneurysm to develop. The appearance 18 months after operation is shown in Figure 13. The patient has been completely relieved of his symptoms and appears to be cured.

I considered placing a free graft of parietal pericardium over the tumor bed, as illustrated in Figure 14, but felt that the parietal pericardium would become sealed to the tumor bed without placing such a graft. Recently I applied this method in the treatment of an aneurysm of the left ventricle.

DISCUSSION ON TUMORS OF THE HEART

A considerable literature exists on tumors of the heart. Most of these tumors are malignant and offer little or no possibility for surgical removal.



FIG 14—A free graft of parietal pericardium might be applied to the heart for the purpose of reinforcing a weakened area such as might occur after the removal of a tumor or after myocardium has been severely bruised. This procedure might prevent rupture of a ventricle or the formation of an aneurysm of the heart.



FIG 15—Photograph of the heart showing the tumor hanging through the mitral orifice. The tumor was attached by a slender pedicle. (Courtesy of Drs. Dexter and Work.)

Some of the malignant tumors possess pedicles that act as ball-valves in the mitral and tricuspid areas⁸ Even if such obstructive lesions could be removed the tumor would continue to grow However, there are some benign tumors of the heart that seem to offer possibilities of surgical removal I refer to the fibromata or myxomata that arise from the lining of the auricles and occlude the auriculoventricular orifices One of these is illustrated in Figure 15, taken from an article by Dexter and Work⁹ This tumor was a



FIG 16—Drawing of myxoma attached by small pedicle to lining of left auricle The inset shows the tumor lifted from the atrioventricular orifice The pedicle was one centimeter in diameter Removal of this tumor by operation seems to be within the realm of possibility (Courtesy Institute of Pathology, Western Reserve University Cleveland, Ohio)

myxoma and originated from the subendothelial connective tissue of the endocardium of the left side of the atrial septum and had prolapsed into the orifice of the mitral valve, where, doubtless, it acted as a ball-valve, preventing the free flow of blood from the left atrium into the ventricle The tumor was a pear-shaped lobulated mass which measured 4.5 by 4.2 by 3.5 cm The tumor was attached by a pedicle and the small end of the tumor hung two centimeters below the valve ring The tumor was soft and gelatinous Another myxoma of the heart is illustrated in Figure 16 The left auricle was completely filled with an irregular nodular mass which protruded into the

atrioventricular opening. The mass was soft and jelly-like. It was attached to the auricular wall by a pedicle one centimeter in diameter. Weakness appeared two years before death. The left auricle became dilated. Circulatory failure developed. The clinical diagnosis was rheumatic heart disease and mitral stenosis. This patient showed embolic phenomena, and infarcts of spleen, kidneys, lungs and brain were found. These two cases appeared in Cleveland within a period of five years. Perhaps they are not so rare. A fibroma of the heart was reported by Houck and Bennett¹⁰. This tumor obstructed the mitral orifice into which it protruded and out of which it could be displaced. It was attached to the septum by a pedicle five millimeters in diameter. It was edematous, soft and jelly-like. It was not invasive. The tumor measured 4.5 x 4 x 3 cm. Strouse¹¹ reported a somewhat similar tumor in the right auricle, a myxoma, attached to the septum, and measuring 8 x 10 x 10 cm. This patient was intermittently well and ill, as though the tumor intermittently obstructed the circulation. The tumor was soft, jelly-like, and was not invasive. Another similar myxoma of the left auricle, attached to the septum, measuring 3.5 x 4 cm, was reported by Bennett, Konigsberg and Dublin¹². It had a rubbery consistency, was relatively avascular, and was not malignant.

No doubt other similar benign tumors of the heart could be found in the literature. It would appear that the correct clinical diagnosis of a benign lesion of the heart, with the exception of my case, has not yet been made during life, and none of them have been operated upon. It seems to me that these soft, jelly-like, benign lesions arising from the endocardium could be removed by operation. It might be possible to remove them in much the same way as the neurosurgeon removes a soft glioma of the brain by means of strong suction. It does not appear to be impossible to insert a glass suction tube into the auricle for this purpose. It might even be possible to open the auricle and take out the tumor. We know that the circulation can be stopped for a period of three to five minutes without inflicting permanent damage to the brain. The great veins to the heart might be occluded for a few minutes. It is hoped that the method developed by John Gibbon,¹³ of Philadelphia, might be applied to these surgical problems. Gibbon's method consists of removing venous blood, oxygenating the blood and delivering it to the brain under pressure. The heart has been taken out of the circulation for as long as 42 minutes in the cat, with recovery. This method seems to have great promise for the future.

While no other benign lesion of the heart has been recognized clinically or operated upon, it should be mentioned that Shelburne¹⁴ took one step toward the surgical treatment of a malignant tumor of the heart. A correct clinical diagnosis was made by Shelburne, and this appears to be the first time that this has been done for a primary malignant lesion of the heart. Hemorrhage into the pericardial cavity took place in this patient and the blood was evacuated by operation. None of the tumor was removed.

SUMMARY

A case of intrapericardial teratoma is reported. There are only a few cases reported in the literature. This appears to be the first and only case in which the lesion was removed by operation. The lesion was completely removed, and the patient has been cured.

A case of a tumor-like mass located in the wall of the left ventricle is reported. The identity of the lesion has not been established. It was probably not a true neoplasm. This appears to be the first time that a benign lesion of the heart has been recognized clinically, and the only case in which the removal of the lesion has been carried out. The patient has had a good result, 18 months after operation. An aneurysm of the left ventricle has not developed. Benign tumors of the heart were discussed in relation to the problem of removal. A method of grafting a segment of pericardium or fascia lata upon the ventricle to reinforce the weakened area and to prevent the formation of an aneurysm is illustrated.

REFERENCES

- ¹ Hedblom, C. A. Intrathoracic Dermoid Cysts and Teratomata. Report of Six Personal Cases, and 185 Cases Collected from the Literature. *J Thoracic Surg*, **3**, 22, 1933.
- King, E. S. J. *Surgery of the Heart*. The Williams and Wilkins Company, 1941.
- ² Somolinos, G. Teratoma di pericardio. *Arch Cardiol y Hemat*, **17**, 152, 1936.
- ³ Joel, J. Ein Teratom auf der Arteria pulmonalis innerhalb des Herzbeutels. *Wiener Arch f path Anat*, **122**, 381, 1890.
- ⁴ Mouat, T. B. Case of Suppurating Dermoid of the Mediastinum. *Brit M J*, **1**, 90, 1909.
- ⁵ Grimm, H. W. Mediastinal Teratoma. *Radiology*, **8**, 438, 1927.
- ⁶ Jellen, J., and Fisher, W. E. Intrapericardial Teratoma. *Am J Dis Child*, **51**, 1397, 1936.
- ⁷ Hoffman, P. D. Tumor of the Left Auricle. *New York Pathological Proc*, **21**, 85, 1921.
- Pawlowski, R. A. Beitrag zum Studien der Symptomatologie der Neubildungen des Herzens. Polypose Neubildungen des linken Vorhofs. *Berl klin Wchnschr*, **32**, 393, 1895.
- Wainwright, C. W. Intracardiac Tumor Producing Signs of Valvular Heart Disease. *Bull Johns Hopkins Hosp*, **63**, 187, 1938.
- ⁸ Dexter, R., and Work, J. L. Myxoma of the Heart. *Arch Path*, **32**, 995, 1941.
- ⁹ Houck, G. H., and Bennett, G. A. Polypoid Fibroma of the Left Auricle (So-called Cardiac Myxoma) Causing a Ball-valve Action. *Am Heart J*, **5**, 787, 1930.
- ¹⁰ Strouse, S. Primary Benign Tumor of the Heart of 43 Years' Duration. *Arch Int Med*, **62**, 401, 1938.
- ¹¹ Bennett, D. W., Konigsberg, J., and Dublin, W. Primary Tumor of the Heart Producing an Unusual Cardiac Shadow in the Roentgenogram. Report of a Case. *Am Heart J*, **16**, 117, 1938.
- ¹² Weinberger, L. M., Gibbon, M. H., and Gibbon, J. H., Jr. Temporary Arrest of the Circulation to the Central Nervous System, Physiologic Effects. *Arch Neurol & Psychiat*, **43**, 615, 1940.
- ¹³ Shelburne, S. Primary Tumors of the Heart. Special Reference to Certain Features which Led to a Logical and Correct Diagnosis before Death. *Ann Int Med*, **9**, 340, 1935.

POSTOPERATIVE THROMBO-EMBOLIZATION

The Platelet Count and the Prothrombin Time After Surgical Operations A Simple Method for Detecting Reductions and Elevations of the Prothrombin Concentration (or Activity) of the Blood Plasma

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IT HAS BEEN DEMONSTRATED that postoperative thrombosis and embolism may be prevented by the use of the anticoagulant heparin^{1, 2} Because this substance possesses certain objectionable features, such as its cost, the necessity for continued intravenous administration, and adverse reactions in some patients, it was considered possible that other anticoagulants might, under certain conditions, be more preferable

In a recent series of publications, K P Link, and his associates,^{3, 4, 5, 6, 7} of the Wisconsin Experiment Station, revealed an outstanding work in which they isolated, identified, and synthesized the causative agent of the hemorrhagic "Sweet Clover Disease of Cattle"^{8, 9, 10, 11} This substance—3, 3' methylenebis (4-hydroxycoumarin)—in adequate dosage decreases the coagulability of the blood *in vivo* by reducing its prothrombin level (or activity) Before applying this material as a possible prophylactic agent against postoperative thrombo-emboli it was desirable to investigate, first, the coagulability of the blood and particularly the prothrombin times during the postoperative periods

Changes in the clotting mechanism of the blood, as expressed by alterations in the platelet count, after surgical operations and parturition, have been demonstrated by Hueck,¹² and Dawbarn, Earlam and Evans¹³ They showed that there is initially a temporary reduction in thrombocytes, followed on or about the sixth day by a more or less sharp rise, after which the count gradually recedes to normal on the tenth to the fourteenth day It was emphasized that most of the fatal cases of thrombo-embolization occurred during this interval of thrombocytosis

We have repeated these studies in 23 patients after surgery and, in addition, have studied the prothrombin time of the plasma

Complete blood counts were made at least every third day The platelet count and coagulation time and the plasma prothrombin time were estimated daily, except Sunday

The technic for estimation of the prothrombin time was that described by Link, and his students (based on the single-stage method of Quick¹⁶), ex-

cept that Russell snake-venom^{14, 15} was substituted for the thromboplastin-calcium chloride mixture, as prepared by Link, and his coworkers^{4*}

Briefly stated, the method is as follows. Four point five cubic centimeters of freshly drawn venous blood are added to 0.5 cc M/10 sodium oxalate. Clear plasma is obtained by centrifuging. One-tenth cubic centimeter of plasma is added to 0.1 cc of venom and placed in a constant temperature bath for five minutes. To this is quickly added 0.1 cc M/40 calcium chloride, which has been kept at the same temperature, and the time elapsing before fibrin clot formation is noted with a stop-watch. The same procedure is then repeated with 0.1 cc of 25 per cent plasma in place of whole plasma.

Dilution of one part of whole plasma with three parts normal salt solution permits of a clearly detectable and satisfactorily reproducible end-point. It has been found that, in man, higher dilutions, especially when the prothrombin time is considerably prolonged, often do not^{**}

It has been found, with this method and using venom, that the average difference between the prothrombin time of whole and of 25 per cent plasma obtained from apparently normal individuals is about ten seconds[†]. It has been found also, that prolongation of this difference occurs when the prothrombin level (or activity) of the blood becomes reduced below normal, and that shortening of this difference takes place as the concentration (or activity) of prothrombin in the blood increases. A state of hyperprothrombinemia is, theoretically, a possibility. It appears that a lessening of the difference, as revealed in this method below that observed in normal plasmas might indicate such a condition¹⁷.

This report embraces the above detailed studies on 23 postoperative patients.

DATA

RESULTS On the first to about the fourth day after surgical operations the platelet count was relatively decreased in eight of 23 cases. Commencing about the fifth or sixth day, and as late as the fourteenth day postoperative, an increase in the circulating thrombocytes was observed in 15 cases, varying in degree from about one and one-half to about twice the count prior to the time this elevation commenced. The duration of this platelet rise was variable, the shortest being two days and the longest a fortnight. The coagulation time, as estimated by the three-tube method of Lee and White,¹⁸ showed little deviation from the normal (Chart 1).

* In the present series venom was used exclusively. In a subsequent study the thromboplastin-calcium chloride mixture of Link, *et al.*,⁴ is being used.

** This applies when venom is used. It has been found that 12.5 per cent plasma is better suited for this estimation when Link's thromboplastin-calcium chloride mixture is used.

† Each laboratory should determine this value by the particular method used. By the technic described, the arithmetic mean has been found to be 10.5 sec and the standard deviation $s.d. \pm 2.4$, the minimum 7, and the maximum 16.5.

In four of the postoperative patients who showed a fall in the platelet count after operation (and seven others who did not) there was also observed, concomitantly, an extension beyond that seen in normal plasma of the difference between the prothrombin time of whole and of 25 per cent plasma. This latter was due, in most part, to a greater prolongation of the 25 per cent plasma prothrombin time in relation to that of the whole plasma. When the

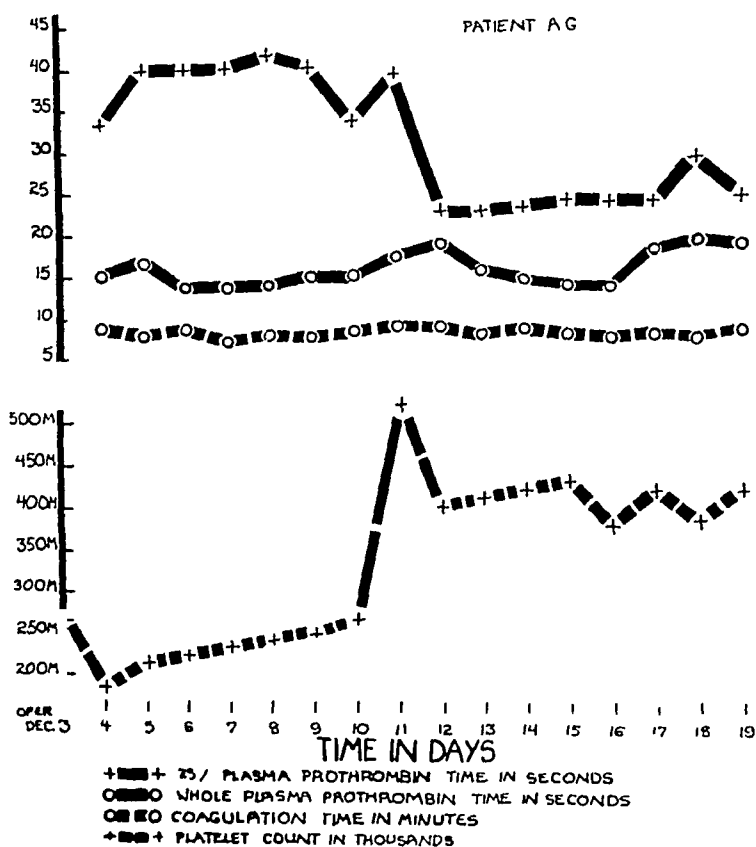


CHART 1—The platelet count, coagulation time and prothrombin times of a case, illustrating the initial fall in platelet count and its subsequent rise on the seventh (7th) day after operation. The coagulation time (Lee and White method) changed slightly. The widened initial difference in prothrombin time between whole and 25 per cent is shortened simultaneously with the thrombocytosis.

circulating thrombocytes increased, this difference shortened due, chiefly, to a reduction in the 25 per cent plasma prothrombin time. This was noted in 14 cases, in three of which, however, no significant alteration in the platelet count occurred. In three cases, in which the difference fell to below three seconds on two successive days thrombophlebitis was found to be present and in two of these, pulmonary infarction occurred. No change in the blood counts was observed which could be correlated with the alterations in the platelets and prothrombin time described above (Chart 2).

DISCUSSION—The precise mechanism responsible for the initial fall in the platelet count following surgical operations is not clear. Anesthesia is not the cause, for we have detected it after local as well as general narcosis. Others have made the same observations¹³. It has been suggested that an

TABLE I
STATISTICAL DATA OBTAINED IN 23 POSTOPERATIVE PATIENTS

Number	Patient	Sex	Age	Platelets (in thousands)				Difference between Whole and 25% Plasma Prothrombin Time (in seconds)				Operation	
				Initial	Post- Fall *	Day Post- oper	Rise*	Initial	Post- Diff *	Day Post- oper	Re- duced		Day Post- oper
1	A G	M	27	260 to 190	1	260 to 510	7	19	1	4	7	Herniotomy	
2	B F	I	32			220 to 360	5	40	1	15	5	Appendicectomy	
3	B A	F	52					17	1	5	3	Pelvic repair	
4	L P	I	40			240 to 420	1	20	1	6	4	Appendicectomy	
5	H B	M	30			220 to 330	5	15	1	5	5	Appendicectomy	
6	A B	M	39			400 to 560	3	15	1	2	3	Amputation gangrene	
7	J P	M	41			190 to 360	4	9	1	1	4	Hemorrhoidectomy	
8	M D	M	38			260 to 490	8	10	1	8	4	Appendicectomy	
9	O A	M	72	493 to 305	3	300 to 400	6	30	3	10	6	Revision of stump	
10	H C	M	29	300 to 240	3	220 to 340	7	21	3	4	5	6	Herniotomy
11	S C	M	32			208 to 360	12	14		2	14	Herniotomy first seen on 10th day post oper	
12	J C	M	22	230 to 150	5	180 to 367	10	10	1			Open reduction— Kirschner Wire	
13	G L	M	27			220 to 290	4	9	1	4	4	Hydrocele	
14	M B	I	16			240 to 300	7	8	1	2	2	Appendicectomy— 103° fever on 2nd day postoper only	
15	A R	F	50			260 to 360	2	25	1	13	2	Appendicectomy	
16	H G	M	29					20	2	5	7	Herniotomy	
17	F D	M	27			260 to 390	4	7	2	8	4	Open reduction— Kirschner Wire	
18	H F	F	36							2	11	Pelvic repair Throm- boemboli first seen on 10th day postoper	
19	M S	F	40					8	2			Appendicectomy	
20	A K	M	42	225 to 170	2							Appendicectomy	
21	M K	M	49	309 to 215	3							Gastrostomy	
22	C McC	M	27	300 to 250	2							Hemorrhoidectomy	
23	P R	M	30	419 to 202	2			16	5	2		Skin graft	

* Blank squares indicate no change

agent is liberated which depresses the thrombocytes along with other constituents of the blood, including the proteins^{12, 23} The concomitant prolongation of the prothrombin time suggests similar inhibitory effects upon the formation or activity of prothrombin This hypoprothrombinemia may be controlled by vitamin K administration None of the patients of the present series had received vitamin K

The explanation for the subsequent thrombocyte and prothrombin increase is lacking. It is important to point out the parallelism that appears to exist between these two coagulation bodies—platelets (thromboplastin) and prothrombin. Whether other related factors such as fibrinogen similarly increase is now being investigated.

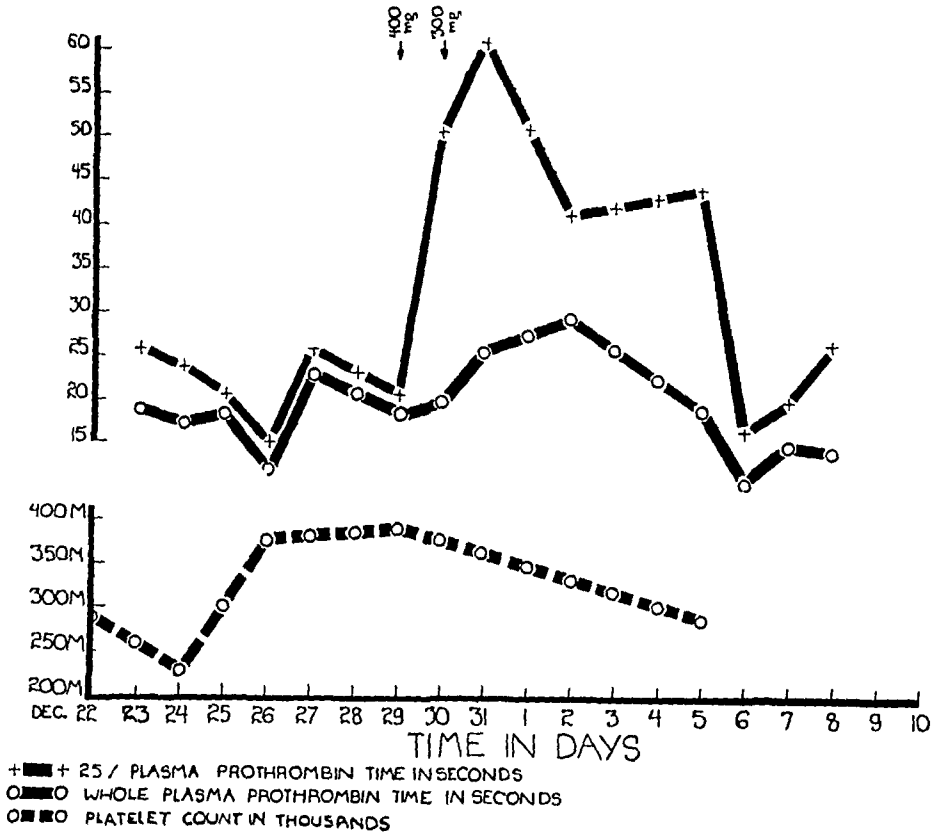


CHART 2—Illustrates marked shortening between whole and 25 per cent plasma prothrombin times immediately preceding pulmonary infarction which occurred on December 27. The dosages noted—400 and 300 mg on December 28, and 29 respectively are of 3, 3' methylenebis (4 hydroxycoumarin) given orally. Note effect upon the prothrombin level (or activity).

Our findings, and those of previous workers,¹²⁻¹ correspond in respect to the thrombocytes. There is some lack of agreement between the coagulation times as observed by us and those of Dawbarn, Earlam and Evans¹ and this is to be explained by difference in method. They used a capillary-tube method, hence their specimens of blood might have been contaminated by tissue juices, which are known to possess coagulating properties. In any event as estimated by the method at hand, the whole blood coagulation was not appreciably altered beyond the limits of normalcy.

The difference in prothrombin time between that of whole and 25 per cent plasma appears to be significant. Normally there is in the blood an excess of prothrombin beyond that needed for normal coagulation.¹⁶ The extent of this excess seems variable in certain diseased states (liver) although under apparently normal conditions it is constant within the limits detectable by the method used here. The whole blood prothrombin time remaining within

normal limits and the difference increasing, the indication appears to be that the excess only is being depleted while the basic essential normal prothrombin level (or activity) is being maintained. However, should the whole plasma prothrombin time also show progressive prolongation it would signify that this plasma prothrombin content (or activity) was also being reduced and might be approaching a hazardous level.*

An inverse relationship between the difference in prothrombin time between that of whole and of 25 per cent plasma, and platelet count, is demonstrable in those postoperative cases in which alterations in the number of circulating thrombocytes was observed. In other words, the prothrombin concentration (or activity) and the platelet count increased *pari passu*. Prothrombin does not have its origin in the platelets²⁴ nor is it necessarily influenced by thrombocytopenia occurring under other conditions. It appears that the tissue of origin of prothrombin (liver?) and of the platelets or the megakaryocytes are similarly affected after surgery.

The data indicate that these substances (prothrombin and thromboplastin) which take part in the process of coagulation of the blood increase in concentration and/or activity commencing about the sixth day after operation. This is the interval when the incidence of postoperative thrombo-embolization is greatest²⁵. It is believed that there is casual relation between these two events. The finding that the concentration (or activity) of prothrombin is greatest (as shown by the shortest differences between the whole and the 25 per cent plasmas) in those instances in which thrombo-embolic phenomena had taken place, might also be interpreted as indicating a possible relationship between these events. Whether there actually occurs a hyperprothrombinemia remains to be further demonstrated. It is also not known whether the change in the blood vessels precedes the increased prothrombin level (or activity) or follows it. The mechanism of blood coagulation involves several reactions. Although these overlap the process of blood clotting is, nevertheless, continuous and progressive. Hence, inhibition at any one stage stops all the succeeding reactions. Thus, the indication for a therapy which is capable of limiting the coagulations of the blood in such a manner becomes apparent. The substance 3, 3' methylenebis (4-hydroxycoumarin) prevents or inactivates prothrombin in man^{20,21}. If this can be administered with adequate safety, and so that the extent of its action can be predicted with some approximation, it might prove appropriate as a preventive against postoperative thrombo-embolization, especially in view of the finding that the prothrombin level (or activity) appears to be increased at the time that thrombosis occurs. It does not appear necessary to administer anticoagulant therapy to every patient after surgery as a routine measure, for the incidence of postoperative thrombo-embolization is about one per cent of major surgical cases.²⁴

* This is especially important in following the effects of dicoumarin therapy.

The procedure being followed by us is as follows. Prothrombin estimations are made daily after surgery. In those instances in which the difference between whole and 25 per cent plasma prothrombin time becomes progressively shortened to below six seconds for two successive days, the dicoumarin compound is given. Its effect is observed by following the prothrombin times (Chart 3).

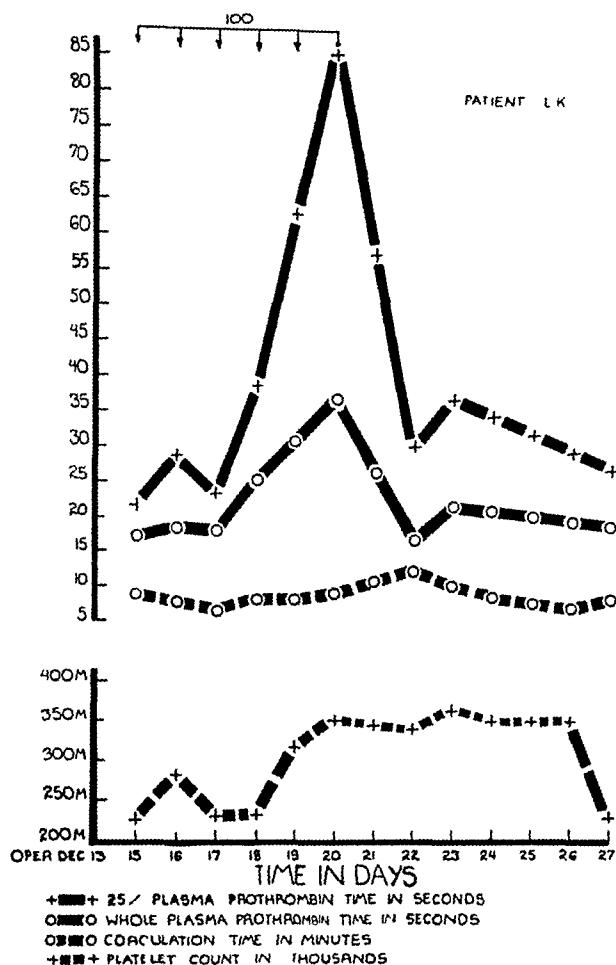


CHART 3—Illustrating the effect of 100 mg daily by mouth for six successive days commencing on the second day after operation of 3,3' methylenebis (4 hydroxycoumarin). There were no complications and no thrombophlebitis in this case.

CONCLUSIONS

Evidence is presented which confirms the findings of previous observers,^{12, 1} that the platelet count may be (1) low during the first three to five days, and (2) elevated commencing about the sixth to tenth day and continuing for from two to 14 days after surgery.

It has been found (similar to reported observations¹⁹) that the prothrombin concentration (or activity) may be low, initially after operation.

In 14 of 23 cases the prothrombin level (or activity) was found to increase, usually concomitantly, with the thrombocytosis occurring on the sixth to tenth day following operation.

In three cases of postoperative thrombophlebitis (two of which also had pulmonary infarction), the prothrombin content (or activity) was highest of all the cases examined. The suggestion is offered that this increase in coagulating substances in the blood is related to the development of postoperative intravascular thrombotic phenomena.

Studies are being made to determine the safety and efficacy of 3, 3' methylenebis (4-hydroxycoumarin) as (1) a prophylactic against postoperative thrombo-embolization, and (2) as a treatment of venous thrombosis and its complications.

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BIBLIOGRAPHY

- ¹ Crafoord, C., and Jorpes, E. Heparin as Prophylactic Against Thrombosis. *J. A. M. A.*, **116**, 2831, June 28, 1941.
- ² Murray, Gordon. Heparin in Surgical Treatment of Blood Vessels. *Arch. of Surg.* **40**, 307, 1940.
- ³ Campbell, H. A., Roberts, W. L., Smith, W. K., and Link, K. P. Studies on the Hemorrhagic Sweet Clover Disease. 1. The Preparation of Hemorrhagic Concentrates. *Jour. Biol. Chem.*, **136**, No. 1, 47, October, 1940.
- ⁴ Campbell, H. A., Smith, W. K., Roberts, W. L., and Link, K. P. Studies on the Hemorrhagic Sweet Clover Disease. 2. The Bioassay of Hemorrhagic Concentrates By Following the Prothrombin Level in the Plasma of Rabbit Blood. *Jour. Biol. Chem.*, **138**, No. 1, 1, 1941.
- ⁵ Campbell, H. A., and Link, K. P. Studies on the Hemorrhagic Sweet Clover Disease. 4. The Isolation and Crystallization of the Hemorrhagic Agent. *Jour. Biol. Chem.*, **138**, No. 1, 21, March, 1941.
- ⁶ Stahmann, M. A., Huebner, C. F., and Link, K. P. Studies on the Hemorrhagic Sweet Clover Disease. 5. Identification and Synthesis of the Hemorrhagic Agent. *Jour. Biol. Chem.*, **138**, No. 2, 513, April, 1941.
- ⁷ Huebner, C. F., and Link, K. P. Studies on the Hemorrhagic Sweet Clover Disease. 6. The Synthesis of the D-Diketone Derived from the Hemorrhagic Agent Through Alkaline Degradation. *Jour. Biol. Chem.*, **138**, No. 2, 529, April, 1941.
- ⁸ Schofield, F. W. Damaged Sweet Clover. The Cause of a New Disease in Cattle Simulating Hemorrhagic Septicemia and Blackleg. *Jour. Am. Vet. M. Assn.*, **64**, 553, February, 1924.
- ⁹ Roderick, L. M. Pathology of Sweet Clover Disease in Cattle. *Jour. Am. Vet. M. Assn.*, **74**, 314, February, 1929.
- ¹⁰ Roderick, L. M. A Problem in the Coagulation of the Blood. Sweet Clover Disease of Cattle. *Am. Jour. Physiol.*, **96**, 413, February, 1931.
- ¹¹ Roderick, L. M., and Schalk, A. L. Studies on Sweet Clover Disease. *N. Dakota Ag. Exp. St. Bull.*, 250, 1931.
- ¹² Hueck, H. Über Untersuchungen der Eiweisskörper des Blutes, sowie Blutplättchen-zählungen, besonders nach Operationen. *Deutsch. med. Wchnschr.*, **51**, 1869, 1925.

- ¹³ Dawbarn, R. V., Earlam, F., and Evans, W. H. The Relation of the Blood Platelets to Thrombosis After Operation and Parturition. *Jour Path and Bact.*, **31**, 833, 1928
- ¹⁴ Fullerton, H. W. Estimation of Prothrombin, A Simplified Method. *Lancet* **2**, 195 1940
- ¹⁵ Page, R. C., and Russell, H. K. Prothrombin Estimation Using Russell Viper Venom. *Jour Lab and Clin Med.*, **26**, 1366, 1941
- ¹⁶ Quick, A. J. The Coagulation Defect in Sweet Clover Disease and in Hemorrhagic Chick Disease of Dietary Origin. *Am Jour Physiol.*, **118**, 260, 1937
- ¹⁷ Shapiro, S., Sherwin, B., Redish, M., and Campbell, H. A. Prothrombin Estimation. A Method and Interpretations. *Proc Soc Exper Biol & Med.*, May, 1942 (in press)
- ¹⁸ Haden, R. L. Principles of Hematology. Lea and Febiger, Philadelphia, 1940, 2nd Edition
- ¹⁹ Rhoads, J. E. Physiological Factors Regulating the Level of the Plasma Prothrombin. *ANNALS OF SURGERY* **112**, 568, October, 1940
- ²⁰ Bingham, J. B., Meyer, O. O., and Pohle, F. J. Studies on the Hemorrhagic Agent 3, 3' Methylenebis (4-Hydroxycoumarin). I. Its Effect on the Prothrombin and Coagulation Time of the Blood of Dogs and Humans. *Am Jour of the Med Sc.* **202**, No. 4, 567, October, 1941
- ²¹ Butt, H. R., Aiken, E. V., Bollman, J. L. A Preparation from Spoiled Sweet Clover Hay 3, 3' Methylenebis (4-Hydroxycoumarin) which prolongs Coagulation and Prothrombin Time of the Blood. Preliminary Report of Experimental and Clinical Studies. *Proc Staff Meetings of Mayo Clinic*, **16**, 388, June 18, 1941
- ²² Barker, N. W., Nygaard, K. K., Walters, W., and Priestley, J. T. A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism. 2. Predisposing Factors. *Proc Staff Meetings of Mayo Clinic*, **16**, 1, January 2, 1941
- ²³ Eagle, H., Johnston, C. G., and Ravdin, I. S. On the Prolonged Coagulation Time Subsequent to Anaphylactic Shock. *Bull, Johns Hopkins Hosp.*, **60**, 428, 1937
- ²⁴ Brinkhous, K. N. Plasma Prothrombin. *Vitamin K. Medicine*, **19**, 329, September, 1940
- ²⁵ Barker, N. W., Nygaards, K. K., Walters, W., and Priestley, J. T. A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism. 3. Time of Occurrence During the Postoperative Period. *Proc Staff Meetings of Mayo Clinic* **16**, 17, January 18, 1941

THROMBOSIS AND GANGRENE OF RIGHT ARM, ASSOCIATED WITH POLYCYTHEMIA VERA ITS RELATION TO "EFFORT THROMBOSIS"

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AN UNUSUAL CASE is herewith reported both because of its own particular interest and because it brings out the occasionally overlooked association of a general disease with a local vascular change. Despite its rarity the case has practical applications.

Case Report—Hosp No 11707 E J F, white male, age 76, was admitted, January 29, 1940, to the Chestnut Hill Hospital, complaining of numbness, tight stiffness, and aching in the right arm. The present illness began eight days before admission, when he noticed these sensations along the inner side of the arm but had no great discomfort or concern till four days later, when redness and swelling ensued, which extended above and below the elbow. A red streak could then be traced halfway to the shoulder. Hot wet dressings of magnesium sulphate solution were applied, without effect however.

The only other complaints were occasional precordial pain and some discomfort from an ulcer in a discolored area above the right ankle. There was also some discharge from an old scar on the right foot. He gave a history of having had typhoid fever and "intermittent fever" at age 26. A partial amputation of the right foot had been performed for an injury 43 years ago. His family and social history had no bearing on his present condition.

Physical Examination—This disclosed a somewhat red-faced, elderly male, surprisingly well preserved for his age. Temperature 98° F, pulse 94, respirations 24. Blood pressure 108/96. His right arm was swollen and reddened from the shoulder to the hand. The pulse at the wrist was good. The arm did not feel hot. No enlarged axillary nodes were palpable. Further examination was negative, except that the legs exhibited brownish pigmented areas above each ankle, an ulcer being present on the right. The right foot had been partly amputated, and the stump had an open area in the scar. Pulses were not palpable in either leg below the popliteals. *Clinical Diagnosis*—Thrombosis or cellulitis of right arm, general arteriosclerosis, particularly marked in the legs.

Course—On the day following admission a blood examination showed Hb 160 per cent (26.5 mg %), R B C 5,750,000, W B C 10,500, P 86 per cent, L 8 per cent, M 4 per cent, and E 2 per cent. Repeated frequently, specimens being taken from various sites, the hemaglobin and red cell values were always well above normal, the highest hemaglobin value being 175 per cent (2-9-'40), and the highest red cell count 8,350,000 (2-12-'40). The only platelet count (3-6-'40), was normal (358,470).

Wet dressings of a saturated solution of magnesium sulphate were applied for the first two days, but the swelling progressed to the shoulder and neck (Fig 1). The diagnosis of polycythemia vera being tentatively made, a medical consultation was asked. At this time the right arm was warm and the radial pulse full and bounding. There was no tenderness. Swelling was present, with pitting on pressure. Blood pressure was approximately the same in both arms. There was bulging of the supraclavicular fossa and the overlying skin was more dusky than on the opposite side. The sternal end of

the right clavicle appeared to be pushed forward. There was fullness and diminution in breath sounds in both the supraclavicular and suprascapular regions. A firm cord-like structure was felt and seen in the supraclavicular region extending up the neck (Fig 2) which did not pulsate. No Horner's syndrome was noted.

The possibility of a sulcus tumor obstructing venous and lymphatic drainage was entertained, which raised the question of interference with pulmonary circulation as the cause of the change in blood count. A roentgenogram (1-31-'40) showed no tumor, aneurysm or sclerosis of pulmonary vessels.

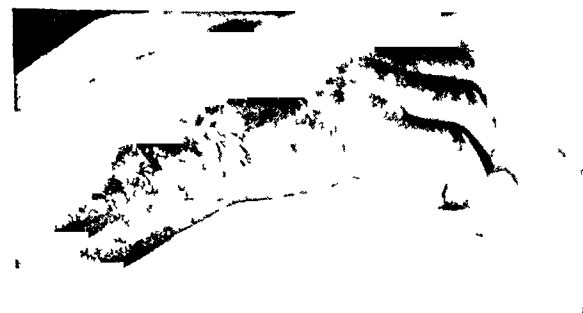


FIG 1—Swelling of arm, shoulder and neck in early stage of condition

FIG 2—"A firm cord like structure is felt in the supraclavicular region extending up the neck"—the external jugular vein

FIG 3—Early signs of wet gangrene in hand

FIG 4—Progression of wet gangrene up forearm

FIG 5—Full extent of gangrenous process

FIG 6—Appearance immediately after operation

The swelling progressed, the upper right quadrant of the chest wall and the right side of the neck being involved. Pulsations at the right wrist were still felt but evidence of early wet gangrene (Fig 3) began to make their appearance in the hand. On 2-7-'40 phenylhydrazine hydrochloride was begun and continued one week. Novocain injections into the cervical sympathetic ganglia were given (2-7-40 and 2-9-40) in an attempt to combat vasospasm and promote vasodilatation in the collateral circulation with little success. General supportive measures were of course being used continuously.

Sterile dressings and dry heat were applied to the right hand and arm, but the gangrene progressed steadily, first involving fingers then hand and forearm (Fig 4). The initial edema and cyanosis of the chest wall, supraclavicular fossa and neck gradually lessened. On 2-14-'40, Dr Hugh Montgomery felt the gangrene to be due to venous and lymphatic blockage. Oscillations recorded by him showed pulsation to be excellent in the uninvolved part of the right arm, demonstrating the freedom from involvement of the upper arterial tree. He suggested culturing of fluid from the blebs which was done and showed (1) Hemolytic and nonhemolytic *Staphylococcus aureus* (2) Nonhemolytic *Staphylococcus albus* (3) Nonhemolytic streptococcus (the organism usually found associated with lymphatic blockage). He also suggested reducing the blood count to normal by phenylhydrazine or bleeding. This drug was again ordered and given for two days, then discontinued. Bleeding was not done, localization of the gangrenous process already having begun, and swelling receding elsewhere.

With this localization of the gangrene, the patient began to improve generally, and from the surgical standpoint it was felt that amputation was inevitable but should wait upon the establishment of a clear line of demarcation.

Various laboratory procedures were carried out during the waiting period. Most of the results were within normal limits. Urine showed no erythrocytes or casts and was otherwise negative. Blood chlorides were low (391 mg per cent on 2-13-'40) the only time taken. Clotting time (2-5-'40) was three minutes. Fragility test on the same day showed hemolysis beginning at 0.48 and complete at 0.36. Blood uric acid was 15 mg per cent, blood sugar 100 mg per cent and the Wassermann and Kahn negative.

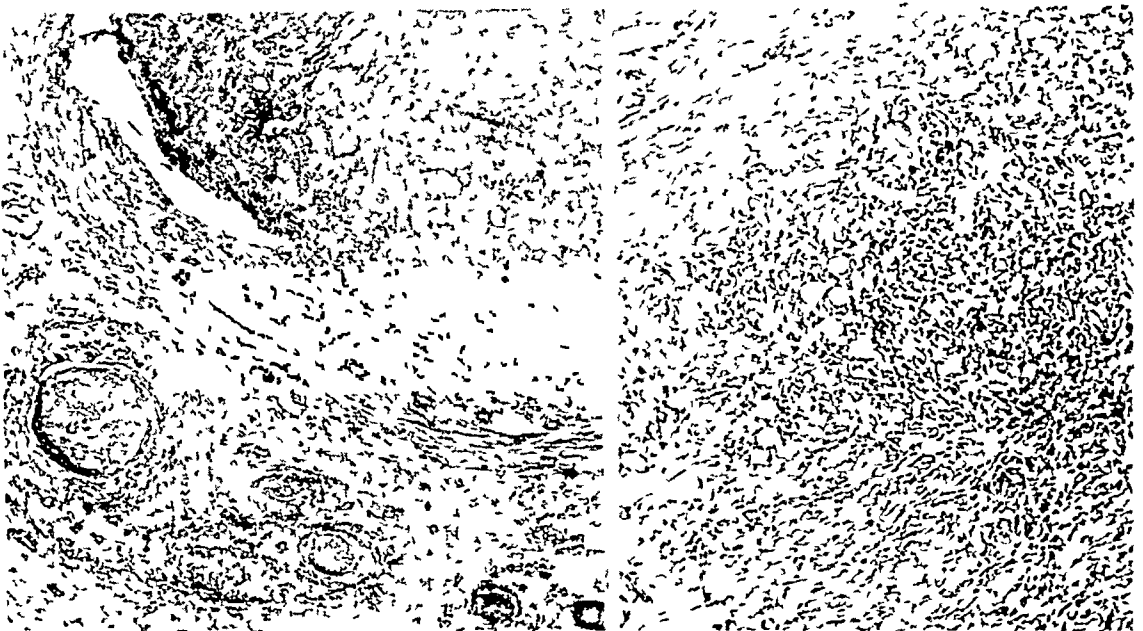
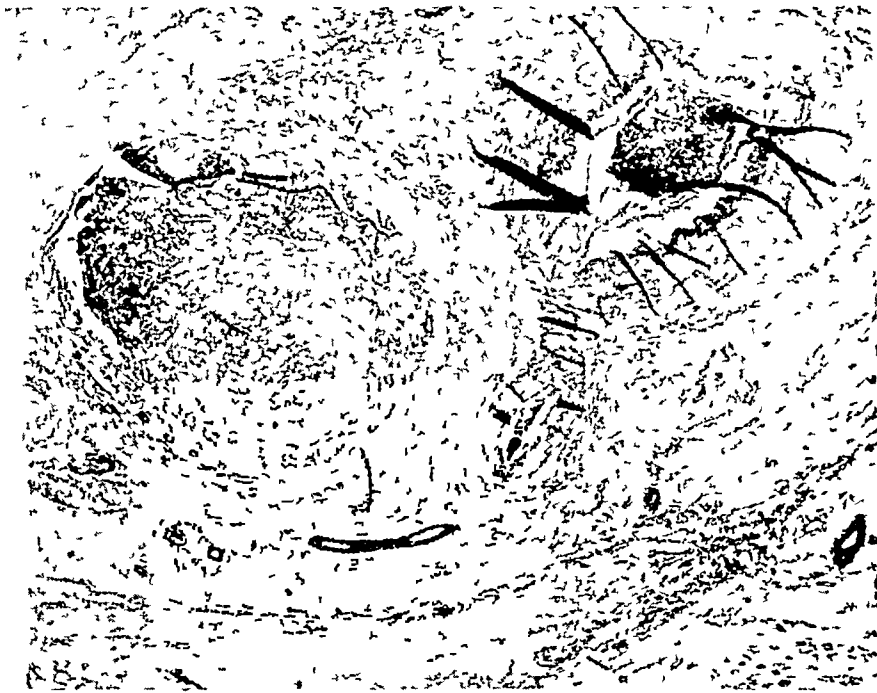
The gangrenous process had arrested itself at midforearm (Fig 5) by 3-30-'40 60 days after onset. On that day with the patient under gas-ether anesthesia an incision was made following the line of demarcation in the midforearm, going through all soft tissue down to the bones. By so doing a flexor surface flap was made. Bleeding was copious (just proximal to the line of demarcation) from both the radial and ulnar arteries, which were clamped and tied. Periosteum on both radius and ulna was raised and stripped upward and both bones were sawed through at the junction of the upper and middle thirds of the arm. The remaining bleeding vessels were ligated and the lower flap was turned up and sewn to the upper by a few through-and-through sutures of silkworm gut (Fig 6). The patient stood the operation well and had a fairly smooth postoperative course. There was some infection of the stump, but of a nonvirulent and well localized type. It took about 12 weeks before healing was complete. Generally the patient was definitely improved after the amputation. His blood count three days later showed Hb 78 per cent RBC 3,910,000 where a week before it had been Hb 11, per cent RBC 5,170,000. It remained at this lower level until discharged (4-29-'40).

Examination of severed hand and lower arm showed general tissue necrosis and thrombosis of veins and arteries as well as some perivascular inflammatory changes.

Following discharge the patient attended the Clinic and his arm as stated gradually healed. No evidence of the recent involvement remained in the upper arm. The cord-like external jugular had returned to normal. The swelling and cyanosis in the shoulder and chest had disappeared. He did have some more trouble with his leg ulcers however. Also, the stump of the right foot seemed more open but in general he was in excellent condition.

In the course of a few more weeks the blood count again reached its former high level and he was readmitted to the hospital (8-2-'40). At this time his spleen was definitely enlarged and palpable. Sudden death occurred (8-31-'40). At autopsy, the following significant findings were noted: (1) Coronary thrombosis with myocardial infarction. (2) Bone marrow showing erythroblastic hyperplasia. (3) Splenic enlargement. (4) A well healed stump of the right forearm. *Pathologic Diagnosis* 1 Polycythemia vera 2 Coronary embolism.

VII



VIII

IX

FIG. 7 —Radial artery and vein. Note almost complete organization of thrombus in vein while artery still shows some unorganized clot in its lumen. This points to the venous origin of the process and the retrograde course of the clotting.

FIG. 8 —Involvement of smaller veins in the complete thrombosis is seen. These are on the periphery of the radial vein and while probably not true vasa vasorum may have received the flow from those vessels. The small arterial channels are all partly open (loose clot may have been washed out).

FIG. 9 —Definite subacute and chronic inflammatory reaction in tissue adjacent to artery and vein. The apparently open lymph spaces are really fat cells whose contents have been dissolved. Few really open lymph spaces are visible.

Discussion—Thrombosis is not at all unusual as a complication of polycythemia vera (Vaquez's or Osler's disease). In fact, about one-third to one-half of the deaths ascribed to this disease are traceable to thromboses of mesenteric, cerebral, coronary or other vessels. But the involvement of the veins of an upper extremity is extremely rare. Stover and Herrell,¹ of the Mayo Clinic, report one such case which almost paralleled our own, and in reviewing the literature they found only one other case resembling theirs, that cited by F. Parkes Weber,² which was really a widespread thrombosis involving both arms and both legs. An article on the 'Vascular Complications of Polycythemia' by Norman and Allen,³ contains no reference to thromboses in the arm, nor does a more recent article by Zeiter.⁴ There are, however, other references to thrombosis of vessels in the upper extremity in association with polycythemia vera in the European literature. Interest in the condition known as "effort thrombosis" began there with the first description of it by von Schrotter,⁵ in 1884 and its continued study since has led to the finding of polycythemia in association with some of the cases. Lohr⁶ reports six cases of thrombosis in the upper extremity. In two of these polycythemia was definitely present, in two more its presence was suspected. In the last two studies were too incomplete to establish it or rule it out. He cites the association of these two conditions in one case reported by Winterstem,⁷ and in three cases by Julius Bauer.⁸ The above cases plus the Mayo case and our own account for eight definite instances where polycythemia and a thrombosis in the upper extremity occurred concomitantly. There are probably more. Our case has the questionable distinction of being the only one in which the process went on to gangrene formation resulting in partial loss of the limb.

Thrombosis of the axillary or subclavian veins from other causes is not uncommon. J. R. Veal⁹ covers this subject of thrombosis in the upper extremity very thoroughly and reports 17 cases—none, however, in association with polycythemia vera. He divides his cases into I. Primary—(A) Thrombophlebitis (bacterial), and (B) Phlebothrombosis (nonbacterial, traumatic or effort thrombosis). II. Secondary—(A) Thrombophlebitis from regional infection, and (B) thromboses from malignancies of the axilla and chest. We quote this logical classification in order to indicate that our present case would fall under group I-B, and to point out its possible relationship to that other condition listed under the same heading "effort thrombosis"—a thrombosis accompanied by a fairly massive swelling of the involved part following some slight trauma, unusual effort or "inappropriate movement." We suggest the possibility, at least, of the presence of polycythemia, often unrecognized, as an underlying factor in some of these cases of "effort thrombosis," where one is often hard put to trace even the slightest abnormal effort as a precursor of the lesion. This suggestion is not original with us, the theory having been advanced very definitely by Lohr,⁶ in 1934. But his suggestion seems to have been overlooked by sub-

sequent writers on the subject. We hold his theory to be of prime importance and worthy of careful attention in the study of future cases of a condition so little understood that Matas¹⁰ describes it as "a complex syndrome of polyvalent causation." Matas also gives a clue as to why polycythemia has not been found more often when he writes "*in the few cases in which careful hematologic studies have been made there are no notable blood changes*———" Again, one must remember that the blood count and hemoglobin values vary from time to time in polycythemia, and if a routine count be taken at a time when these values are at or near normal, polycythemia may not be suspected. For example, in one of Lohr's⁶ well established and thoroughly studied cases with true polycythemia the counts and hemoglobins were normal on isolated occasions. Again (as was the case during our patient's first admission), the elevated erythrocyte count and hemoglobin percentage may not be supported by other findings confirmatory of the diagnosis of true polycythemia and one may not feel justified in making such a diagnosis. However, it is coming to be more and more recognized that a latent or unrecognized polycythemia vera may be present in obscure cases of peripheral vascular disease—chronic leg ulcers, acrocyanosis, *etc.*, as pointed out by Dameshek and Henstell¹¹ in an excellent article on the diagnosis of polycythemia. So, until the condition of "effort thrombosis" becomes more clearly understood we believe a thorough search should be made in every case for polycythemia.

Pathology—With the overabundance of erythrocytes and with hematocrit values well above normal, the viscosity of the blood in polycythemia vera is increased and the rate of flow probably reduced. Add to these predisposing conditions some precipitating factor and thrombosis results. (This may well be some slight trauma or again as here, no exciting cause may be traceable.) Just where the thrombosis occurs is not always detectable and our rather general title "Thrombosis and Gangrene of the Right Arm, *etc.*" is used purposely. In fact, we feel that specific designations of axillary or subclavian thrombosis should be reserved solely for those cases where a demonstrable thrombosis can be found in the vein named and should not be used for general swelling of the arm following a supposed thrombosis which is assumed to be high because the swelling extends to the shoulder or trunk. When thrombosis does set in there follows a marked circulatory disturbance in and about the area drained by the affected segment. A generalized swelling comes on and lymphatic blockage is evident. This may rest upon the Leiche¹² principle of arteriolar spasm as suggested specifically in thrombosis of the arm by Cattalorda,¹³ Roelsen,¹⁴ and by Ochsen¹⁵ in the case of acute phlebitis of the leg, and may lead to secondary edema, lymphedema and stasis. In fact it is suggested by Cattalorda that the whole process may be one of vessel spasm and that no thrombus is necessary to initiate the lesion. Such feeling has arisen from the fact that in some instances axillary and subclavian veins have been exposed with the

intent of excising the affected segment and in some of these there was found no thrombosis at all. Cattalorda had one such experience. Moure and Martin¹⁶ report the same thing, and Roelsen tells of seven cases, three of which were operated upon, but in none of these was anything abnormal found. He feels the whole process may be explained as the result of spasm alone and regards thrombus formation as a complication. The reasoning which localizes the pathology in the subclavian or axillary veins may grow from a fallacious underlying premise of "high swelling-high thrombosis." Is it not possible that in those cases where the explored axillary or subclavian veins were found to be normal that the process did not rest on spasm alone but followed an undiscoverable thrombosis of a vein in the lower arm, forearm or wrist? In our case, when all the secondary manifestations had cleared away, the blockage was clinically demonstrated to be from the midforearm down, yet the swelling in the early stages had extended even over the chest wall. Had our case not gone on to the stage of tissue destruction but had subsided like many others, we, too, would probably be reporting a case of "subclavian vein thrombosis." Venography may prove the means of solving some of these questions.

Many careful studies have been made to explain the true thromboses which occur in the subclavian and axillary veins on an anatomic basis (Willan,¹⁷ Gould and Patey,¹⁸ Lohr,¹⁹ Lowenstein,¹⁹ and Kaplan²⁰). Most of these studies lead to a theory that overstretching with compression and contusion of the vein between clavicle and first rib explains the situation (the subclavius muscle or costocoracoid ligaments exerting the pressure). Some feel the subclavio-axillary valve is damaged. Writers do not stress the role of the lymphatics. None points out that there may be a relationship between the fact that this lesion most often affects the upper right extremity and that the lymphatic system draining the upper right-quarter of the body is constituted differently than the other lymphatics. One thinks of the "right lymphatic duct" receiving the tributaries of the region and emptying into the subclavian vein. Yet, in a definite percentage of cases the three main tributaries of this duct—jugular, mediastino-bronchial and subclavian—do not unite to form it but empty separately into the venous system. In such cases blockage of one such main tributary would be less likely to extend to the others and would show itself by the clinical phenomenon of swelling limited to the part drained by the affected trunk. This we think may have occurred in our patient, for the whole area involved was drained by the subclavian lymphatics—the arm, obviously, the chest wall by the channels accompanying the superior thoracic, long thoracic *etc.* Even the lymphatics accompanying the external jugular vein, so prominently involved here, follow this vessel to the subclavian lymphatics and are not a part of the internal jugular system of lymphatics. This would account for the pronounced cord-like swelling along the external jugular without swellings of the other parts of the neck, or face as seen in our patient. What the mechanism of this lymphatic

blockage is we cannot say absolutely, but it does seem to be the major cause of the alarming swelling. Microscopic sections made of the radial artery and veins in our case (Fig 9) show definite subacute and chronic inflammatory changes in the periarterial and perivenous tissues.

As to the gangrene formation, it was due, no doubt, to the backing up of resistance to the flow of arterial blood until tissues no longer received adequate nourishment. The gangrenous process then extended up the arterial tree a certain distance, aided, we feel sure, by the arteriosclerosis present. That the original thrombosis was, in itself, massive enough to accomplish all this is unlikely but that a pernicious progressive occlusive process was initiated is more plausible. Collateral vessels were probably narrowed by spasm, their own blood supply impeded through the pressure of the lymphedema on their vasa vasorum and, finally, their sluggish stream came to the clotting point. The mechanics of "wet gangrene," a subject not greatly discussed in recent years, is adequately dealt with by Audier and Hamoric.²¹

Symptoms and Signs—The symptoms in our case were very similar to those in the Mayo case—painless swelling, slight tenderness, deep red cyanosis, with gradual extension of the process to the shoulder and chest wall were common to both. Cord-like prominence of the veins mentioned by Stover and Heibel¹ was noted only in the external jugular by us. Pulses at the wrist remained normal until the gangrenous process shut them off. Writing of axillary and subclavian vein thrombosis, Veal¹⁹ gives as typical the following signs and symptoms no matter what the underlying cause. Pain in the arm and shoulder (not definite in our case), massive pitting edema of the entire extremity, weakness and partial loss of function of the arm, preservation of the radial pulse, elevation of the systolic pressure on the affected side (in ours pressures were equal), palpable, tender cord-like swelling along the course of the brachial, basilic and axillary veins (external jugular here), and marked elevation of the venous pressure and a decrease in the oxygen content of the venous blood of the affected arm (these latter two points not checked in our case).

We do not presume to discuss the diagnosis of the general disease—polycythemia vera—other than to stress the fact that not all signs are present in every case, and if one finds a persistently high erythrocyte count and hemoglobin value it may be practical to assume that the disease is present. Splenic enlargement for example was not demonstrable in our patient while he suffered his thrombosis in the right arm but was present a few months later. Increase in platelets was not found at the height of his red cell increase. The fragility of the cell was within normal limits—the described increased resistance to hemolysis not being shown. Yet the autopsy findings of splenic enlargement, terminal coronary thrombosis and red bone marrow hyperplasia firmly establish this as a true case of Vaquez's disease. One of the more recently discussed²² causes of pseudopolycythemia vera—sclerosis of pulmonary vessels—was eliminated here by a chest roentgenogram which showed none of the characteristic sclerosis.

Treatment—What has been said about the diagnosis of the general condition has a direct bearing on treatment. Although injection of the sympathetic ganglia, excision of affected vein segments, paravenous and periarterial sympathectomies have been tried, it is rather generally agreed (Veal, Matas, Roelsen) that the treatment of thrombosis is supportive—elevation, rest, moist warm applications *etc.* In other words, one does little but promote circulation and await the reestablishment of ample venous return through collateral channels. But in our case this was not enough, probably because of the markedly increased viscosity and slowing of flow which accompanies polycythemia vera, and which tends to promote an extension of the thrombus formation into those channels which ordinarily might serve as detours (Fig 8). In the Mayo case, prompt recognition of the general disease and ample blood-letting (5,250 cc over an eight-day period) contributed to the saving of the limb. Perhaps (although we cannot be sure) this procedure would have resulted in a better outcome in our patient. However, in our own defense, we must point out that Lohr⁶ had two cases of polycythemia vera with the thrombosis syndrome in the arms, and in neither case did gangrene result even though the treatment was entirely “supportive.” The point of difference was that these two patients were young and otherwise healthy, while our patient was old and markedly sclerotic.

If gangrene is inevitable it is wise, we believe, to await the line of demarcation and then amputate. The way our flaps healed, despite an already present infection showed that circulation to the line of tissue change was quite competent.

Liability—Of practical importance from another standpoint is the interesting fact that “effort thrombosis” coming on after trauma—even the slightest—suffered at work has been adjudged a compensable accident. Louisiana established this precedent the courts submitting the question for decision to Dr. Rudolph Matas, who came to this conclusion after a thorough study of the subject. If there was no preceding trauma, however, Matas felt no liability existed. Since the question of the presence of a predisposing factor would be of great importance in settling such a question we feel that here is one other reason for making a thorough search for polycythemia vera in all cases of so-called “effort thrombosis.”

SUMMARY AND CONCLUSIONS

1. A case of thrombosis in the vessels of the arm accompanied by massive swelling extending to the chest wall and neck in a patient with polycythemia vera is reported.

2. Seven other such cases have been traced in the literature. Our case was the only one in which the process resulted in gangrene.

3. We believe as did Lohr⁶ that an unrecognized polycythemia vera may underlie a certain number of cases of so-called “effort thrombosis.” It should be carefully sought for in each future case to prove or disprove this contention.

4 Thrombosis of vessels in the lower arm forearm or wrist plus the extensive lymphatic stasis which follows may explain many cases incorrectly designated as examples of subclavian or axillary thrombosis

5 In a patient suffering from a thrombosis, increased red cell and hemoglobin values call for therapeutic blood-letting, regardless of whether the condition can be accurately diagnosed as a true polycythemia or not

6 Since the question of compensation may arise in cases of 'effort thrombosis' it is well to establish the presence or absence of polycythemia vera in such cases

REFERENCES

- ¹ Stover, L, and Herrick, W E Extensive Thrombosis of the Right Subclavian and Axillary Veins Associated with Thrombophlebitis, Lymphedema, and Polycythemia Vera Proc Staff Meet Mayo Clinic 15, 817, 1940
- ² Parkes, Weber, F Polycythemia, Erythrocytosis and Erythaemia (Vaquez-Osler Disease) New York, Paul B Hoeber, 1922, p 148
- ³ Norman, I L, and Allen, E V The Vascular Complications of Polycythemia Am Heart Jour, 13, 257, 1937
- ⁴ Zeiter, W J Peripheral Vascular Disease in Polycythemia Vera Med Clin North Am, 24, 485, 1940
- von Schrotter Nothnagle Handbuch der Pathologie und Therapie, Bc, 15, 1884
- ⁶ Lohr, W Deutsch Ztsch f Chir, 214, 263, 1929
- ^{7, 8} Quoted by Lohr, W ⁶
- ⁹ Veal, J R Thrombosis of the Axillary and Subclavian Veins Am Jour Med Sc, 200, 27, 1940
- ¹⁰ Matas, Rudolph So-called Primary Thrombosis of the Axillary Vein, Caused by Strain Am Jour Surg 24, 642, 1934
- ¹¹ Dameshek, W, and Henstell, H The Diagnosis of Polycythemia Ann Int Med, 13, 1360, 1940
- ¹² Leiche, R, and Kunhn, J Immediate Treatment of Postoperative Phlebitis by Novocaine Infiltration of the Lumbar Sympathetics Presse Med, 42, 1481, 1934
- ¹³ Cattalorda, J Lyon Chir, 29, 169, 1932
- ¹⁴ Roelsen, E So-called Axillary and Subclavicular Traumatic Thrombosis Lyon Chir, 36, 385, 1939
- ¹⁵ Ochsner, A, and DeBakey, M Treatment of Thrombophlebitis by Novocaine Block of Sympathetics Surgery 5, 491, 1939
- ¹⁶ Quoted by Cattalorda¹³
- ¹⁷ Willan, R J Edinburgh Med Jour, 20, 105, 1918
- ¹⁸ Gould, E P, and Patey, D H Brit Jour Surg, 16, 208, 1928
- ¹⁹ Lowenstein, P S Thrombosis of Axillary Vein JAMA 82, 854, 1924
- ²⁰ Kaplan T Thrombosis of the Axillary Vein JAMA, 110, 2059 1938
- ²¹ Audier, M, and Hamorici, H Gangrene of Venous Origin in the Extremities With Special Reference to the Role of Phlebitis and Obliteration Presse Med, 46, 1403, 1938
- ²² Hodes, P J, and Griffin, J Q Chest Roentgenograms in Polycythemia Vera and Polycythemia Secondary to Pulmonary Arteriosclerosis Am Jour Roentgenol, 46, 52 1941

IMMEDIATE AND LATE RESULTS OF PERFORATION OF PEPTIC ULCER

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IN THE 15-YEAR PERIOD, from 1925 to 1940, there have been 57 cases of acute perforation of peptic ulcer admitted to Vanderbilt University Hospital, of which 51 were in the duodenum and six in the stomach

This study was primarily for the purpose of testing the validity of the widespread opinion that if a peptic ulcer perforates, and if the patient recovers after closure of the perforation, subsequent permanent healing of the ulcer may be expected to occur. This opinion constituted the basis for a method of treatment of peptic ulcer described by Balfour in 1918. Balfour states "Complete perforation by the cautery point through the center of the crater of the ulcer has been made an essential in the technic because of the clinical fact (drawn attention to early by Mayo, Clairmont and others and now generally recognized) that spontaneous and complete perforation of a gastric ulcer is, presupposing recovery from this accident, quite likely to be followed not only by the cure of the ulcer but by the cure of the patient." In recent textbooks on surgery one finds some difference of opinion as to late results obtained in the patients in question. Christopher has said "Healing of the ulcer occurs after simple purse-string suture in about three-fourths of the cases." More recently, Cutler has written "After three to four days the patient is started on strict medical regimen, which may be continued for an indefinite period, because simple closure of the perforation has not cured the patient of his ulcer or of his tendency to form another." And again, Horsley has written "Frequently after closure of the perforation the lesion appears to heal and the patient remains well, but if symptoms continue, as they do in many cases, the patient can be treated anew as a peptic ulcer case that demands surgery." Grey-Turner estimated that only 50 per cent of their patients with perforations were cured after recovery from the perforation. Lewisohn found that 39 per cent of his patients had persistence of ulcer symptoms. Sullich reported that 70 per cent of his patients were not cured by perforation.

SUMMARY OF CASES

The operative procedure employed in the present series of 57 cases consisted, essentially in removal of all available foreign material in the peritoneal cavity followed by simple closure of the perforation either by purse-string or Lembert sutures.

In three cases the perforation of the ulcer occurred as the first indication to the patients of the presence of gastro-intestinal disorder. Sixteen patients had had symptoms of peptic ulcer for ten years or more prior to the abdominal

PERFORATED PEPTIC ULCER

No of Cases	Av Age	Av Duration of Ulcer Symptoms	Amount of Fluid in Peritoneal Cavity	Wound Infection and Disruption	X-ray Evidence of Air	Size of Perforation	Deaths
			37 large*	12 infections	38 +	10 large†	
57	41 yrs (14-70)	6 3 yrs	18 small	4 disruptions	11 -	47 small	16
			2 not indicated		8—no x-ray		(28 07%)

* Large—greater than 1 000 cc

† Large—greater than 1 cm

catastrophe for which they sought admission to the hospital. None of the patients had adhered to a strict medical regimen of therapy for the ulcer, only eight having had even a short course of formal therapy. The remainder had taken alkali on a bite of food irregularly for relief of abdominal distress.

All the patients gave a history of sudden onset of severe abdominal pain of the nature usually found in this condition. Pain was usually soon followed by vomiting, only eight patients noticed the presence of blood in the vomitus or gave any previous history of either hematemesis or tarry stools. Abdominal rigidity was the rule on examination, but liver dullness was obliterated or impaired in less than one-half of the cases.

No correlation was found to exist between the size of the perforation and the volume of fluid or the presence of air in the peritoneal cavity. Again, no correlation was found between the lapse of time from the time of perforation to the time of operation and the amount of fluid in the peritoneal cavity. The incidence of wound infection increased with the lapse of time between perforation and operative intervention. There were, also, four wound disruptions which showed no relation to lapse of time between perforation and operation or to the occurrence of infection.

The cases have been arbitrarily divided into three groups, according to the number of hours which elapsed from the time of onset of symptoms of perforation to the time of operation.

Group	No of Cases	Av Age	Av Duration of Ulcer Symptoms	Amount of Fluid in Peritoneal Cavity	Wound Infection and Disruption	X-ray Evidence of Air	Size of Perforation	Deaths
A				18 large*	5	20 +	25 small	
0-10 hrs	30	40 yrs	5 8 yrs	10 small	2 disruptions	7 -	5 large†	4
				2 not indicated		3—no x-ray		(13 3%)
B				8 large	3	9 +	9 small	
10-20 hrs	12	44 7 yrs	6 5 yrs	4 small	2 disruptions	2 -	3 large	5
						1—no x-ray		(41 6%)
C				11 large		9 +	13 small	
20+ hrs	15	40 yrs	6 9 yrs	4 small	4	2 -	2 large	7
						4—no x-ray		(46 6%)

* Large—greater than 1 000 cc

† Large—greater than 1 cm

On comparing these groups, one immediately sees that the mortality rate jumps from 13 3 per cent in cases operated upon before ten hours had elapsed

to 45.5 per cent in cases operated upon later than ten hours. No wound infections or disruptions occurred in patients operated upon under three hours.

GASTRIC ULCER

Case No	Age	Duration of Symptoms of Ulcer	Duration of Perforation	Signs of Air	X ray Evidence of Air	Size of Perforation	Wound Infection of Disruption	Duration of Hospitalization	Symptoms Since Operation
72810	23 yrs	1 mo	24 hrs	+	+	Small	0	12 days	+
79346	51 yrs	16 yrs	14 hrs	+	+	Large	0		Expired day of operation
88151	45 yrs	4 yrs	21 hrs	+		6 mm	0	11 days	+
93969	53 yrs	6 yrs	12 hrs	+	+	1.5 cm	Infection	18 days	Died
356	36 yrs	4 yrs	10 hrs		-	2 mm	Disrupted 7th Day	30 days	Asymptomatic 3 yrs Symptoms 12 yrs
95333	20 yrs	1 yr	2½ hrs			2 mm	0	14 days	+

There was no history of hematemesis in any member of this group as contrasted with the cases of duodenal ulcer, in which there were eight patients who vomited blood prior to operation. The patients were all males, averaging age 38.

Since Vanderbilt University Hospital draws its clientele from a large rural area, considerable time elapsed in many cases before the patients presented themselves. Nine of the patients who died postoperatively were seen by their local physicians within a few hours of the time of perforation, were given hypodermic injections, and were not advised to go to the hospital until the following day or later. Of the 57 patients operated upon, 41 left the hospital, and 16 died, a mortality rate of 28.6 per cent as compared to the operative mortality of a collected series of 15,340 cases reported during the last decade of 23.4 per cent (DeBakey). Bager, in reviewing 1,495 cases, found the mortality to be 14.7 per cent for the first six-hour period, 26.5 per cent for the second six-hour period, 47.2 per cent for those operated upon between 12 and 24 hours after perforation, and 65.6 per cent for those operated upon after 24 hours.

The average age of the 16 patients dying was 43.3 years, or approximately the same as that of the group as a whole. In all 16 of these patients a large amount of fluid and gastric content was found in the peritoneal cavity at the time of operation. The amount and time of ingestion of food prior to operation was the most important factor contributing to the amount of fluid in the peritoneal cavity at the time of operation, pyloric obstruction apparently playing no important part in its causation.

In ten patients operated upon within three hours or less after perforation, three patients expired, all three of these perforations occurred while the patients were in the hospital. Also, in all three of these patients there occurred hemorrhage from the ulcer shortly before or at the time of perforation. Two of these cases had been admitted to the Medical Service, one because of

PERFORATED PEPTIC ULCER

bleeding and one because of an increase in the epigastric pain of one week's duration. The third was admitted for a dilatation of a stricture of the anus, which was incident to a hemorrhoidectomy, performed elsewhere, one week previously. In Group A there was only one other patient with history of either hematemesis or tarry stools. This patient was operated upon five hours after perforation, and he too was found to have a large amount of bloody fluid in the peritoneal cavity, likewise the outcome of his case was fatal. These four cases comprised the total deaths occurring in the patients operated upon before the expiration of ten hours after perforation. As shown, there was concomitant hemorrhage in each of these cases. Regarding these four cases, it should also be noted that the perforations varied in size from 1 to 3 cm in diameter.

Case Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Generalized peritonitis																
Broncho pneumonia																
Hemorrhage																
Shock (at operation)																
Peritoneal Abscess																
Pulmonary embolus																
Pyloric obstructions																
Erysipelas abd wall																
Subphrenic abscess																

CHART I

Aside from the three patients mentioned above, there have been two others who perforated while in the hospital, both during gastro-intestinal roentgenologic examinations. Both of these had neither hemorrhage nor obstruction, and both made an uneventful recovery. One of these is a recent case who is not included elsewhere in this study.

In the entire series of 57 patients, there were only eight who gave history of either hematemesis or of tarry stools prior to operation. Three of these have just been discussed, a fourth case was the patient who was mentioned elsewhere herein who suddenly perforated a second time seven years after the first operation. Two more of these patients recovered satisfactorily from the operation but have continued to have ulcer symptoms, without, however, additional bleeding. A seventh member of this group who had recognizable bleeding prior to operation expired, but he was one of those who came to the hospital on the second day following perforation. The eighth member of this group recently returned to the hospital, one year after operation, with a massive hemorrhage as the first indication of persistence of his ulcer. From

these facts it seems clearly evident that the prognosis in peptic ulcer is gravely affected by hemorrhage as concerns both mortality and morbidity

DEATHS

Of the 16 patients who died, postmortem examination was performed in nine. Dual ulcers were found in the duodenum in three of these nine patients. These ulcers were all of the so-called "kissing" variety, in each instance one occurring in the anterior and one in the posterior wall of the duodenum, the perforation was in the ulcer on the anterior wall of the duodenum in each case, in none of these cases had recognizable hemorrhage occurred, either prior to operation, at operation or at autopsy. In another of the autopsied cases, an open artery was found in the margin of the ulcer, which was located on the anterosuperior wall of the first portion of the duodenum.

Course Subsequent to Hospitalization—All of the 41 patients who recovered following operation were traced. Two of these had expired, one of them two and one-half months postoperatively, the cause of death apparently being residual peritoneal infection complicated by empyema, the other patient lived two years, continued to have symptoms, and died of intercurrent infection (pneumonia). Of the remaining 39, seven patients (17.5 per cent) report themselves to be completely free of gastro-intestinal symptoms, while 32 of them (82.5 per cent), including all four of the cases of gastric ulcer who survived, continued to have varying degrees of symptoms of peptic ulcer. These symptoms consisted, essentially, in epigastric pain relieved to some extent by food or alkali, occasional nausea and infrequent vomiting. Very few of these patients have followed strictly any course of medical treatment since operation. Seven of these 32 patients had symptoms ever since operation, while 25 of them have had an asymptomatic period immediately following operation varying from three weeks to six years, averaging 1.8 years. It is interesting, and perhaps informative, to note that the patient reporting the longest asymptomatic period had this period abruptly terminated, without warning, by second perforation of his ulcer.

The seven patients recorded above as being asymptomatic have been so for the following number of years, respectively: seven, seven, four, one, eight, twelve and eight years.

Subsequent Roentgenologic Studies—Sixteen patients out of the 41 who survived have had roentgenologic examinations subsequent to operation, varying in time from 15 days to seven years postoperatively. In every case except one there was found a deformity of the duodenal cap. No distinction can always be made between simple postoperative deformity and that due to a persistent ulcer. The single patient whose gastro-intestinal series was normal had been on a strict ulcer regimen for the eight months preceding the examination, and subsequently he has had a recurrence of his old ulcer symptoms. In three of this group there was some roentgenographic evidence of duodenal

obstruction, which was in agreement with the clinical picture of the cases in question

SUMMARY AND CONCLUSIONS

- (1) Fifty-seven cases of acute perforated peptic ulcer are presented
- (2) The relation of the duration of perforation prior to operation and the hospital course is discussed
- (3) The cause of death and the findings at autopsy are outlined
- (4) The concomitant occurrence of the complication of perforation and bleeding was found to alter greatly the mortality and morbidity
- (5) None of the patients had received adequate medical treatment for ulcer
- (6) The incidence of recurrence of symptoms of ulcer postoperatively, after simple closure of the perforation, was found to be 82.5 per cent
- (7) Following recovery from the operation for closure of a perforated peptic ulcer, the patient should be evaluated anew and treated just as any other case of peptic ulcer

REFERENCES

- ¹ Balfour, D. C. Cautery Excision of Gastric Ulcer. *ANNALS OF SURGERY*, **67**, 726, 1918
- ² Bager, B. Beitrag zur Kenntnis über Vorkommen, Klinik und Behandlung Perforierten Magen- und Duodenalgeschwüren nebst einer Untersuchung über die Spätergebnisse nach Verschiedenen Operationsmethoden. *Acta chir. Scandinav. Suppl. II*, **64**, 5, 1929
- ³ Cohn, R. Repeated Perforations of Peptic Ulcers. *Surgery*, **9**, 688, 1941
- ⁴ Cutler and Zollinger. *Atlas of Surgical Operations*. Pp 57, 1939
- ⁵ Christopher. *Textbook of Surgery*. Pp 1169, 1936
- ⁶ DeBaakey, M. Acute Perforated Gastroduodenal Ulceration. *Surgery*, **8**, 1028, 1940
- ⁷ Horsley and Bigger. *Operative Surgery*, VII. Pp 884
- ⁸ Lewysohn, R. Persistence of Duodenal Ulcer Symptoms after Perforation. *Surg., Gynec., and Obstet.*, **64**, 172, 1937

THE LYMPHATIC AND VENOUS SPREAD OF CARCINOMA OF THE RECTUM^{*}

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AN UNDERSTANDING of the spread of carcinoma of the rectum is essential for the treatment of the disease. Four main routes are possible: (1) By direct extension, (2) by the lymphatics, (3) by the blood stream, and (4) by transplantation through the peritoneal cavity. The second and third routes of spread are the subjects of this report.

LYMPHATIC SPREAD

The clinical observations of Miles,^{1, 2} in 1925, on the lymphatic spread of carcinoma of the rectum and injection studies by French and German anatomists have formed the basis for its present surgical treatment. Recent work by Gilchrist and David,³ and Collier, Kay, and MacIntyre⁴ has thrown further light on the subject. The present study makes use of their methods, and is based on the examination of 75 specimens of the rectum and rectosigmoid removed at operation during the past three years. Sixty-two were removed by abdominoperineal resection, ten by perineal excision, and three by anterior abdominal resection of the rectosigmoid, with either colostomy and inversion of the distal stump or end-to-end anastomosis. In these three cases the superior hemorrhoidal vessels were divided and a wide area of the mesentery was removed. All specimens were cleared by the Spalteholz method, as used by Gilchrist and David, with some slight modifications. All lymph nodes were dissected out, sectioned, and charted on drawings to show their relationship to the tumor and the main blood vessels. By this method, many more lymph nodes were found than would have been possible by less accurate methods. As a result the number of node metastases found was also greatly increased. Metastases were frequently seen in the smallest nodes, with a diameter of only 1-2 mm. Mere size proved to be a completely unreliable guide to the presence or absence of a metastasis in a node.

In this series of 75 cleared specimens, the average number of nodes per specimen was 52. The average number found in specimens removed by abdominoperineal resection was 54, by perineal proctectomy, 31, and by anterior resection, 67. The greatest number found in any one specimen was 124. Metastases were found in 55 per cent of the cases. This incidence is somewhat less than that of 68 per cent reported by Gilchrist and David³ in 25 cleared cases, and that of 64 per cent found by Collier⁴ in 53 cases. It stands out in contrast, however, to that of 36 per cent which was found in a similar series¹⁵ of cases at this hospital, from 1916-1932, in which the clearing tech-

^{*} Read before the New York Surgical Society, January 28, 1942.

nic was not used The incidence in the present series is 19 per cent higher, and demonstrates the value of this method This increase occurred in spite of the fact that more cases in this series were operated upon at an earlier stage, when fewer metastases might be expected Thus, in the 1916-1932 series, 34 per cent of the specimens examined grossly were completely annular, whereas in the present series only 22 per cent were annular That a relationship exists between the extent of bowel circumference involved and the frequency of metastasis will be shown later

TABLE I
INCIDENCE OF NODE METASTASES REPORTED BY PREVIOUS AUTHORS

	No of Specimens	No of Nodes per Specimen	Per Cent with Metast
McVay	100	6	47%
Wood and Wilkie	100	11	51%
Westhues	74 (cleared)	25	59%
Gabriel Dukes and Bussey	100	28	62%
Gilchrist and David	{ 22 25 (cleared)	{ 24 52 }	68%
Coller Kay, and MacIntyre	53 (cleared)	67	64%
Grinnell (1916-1932)	107	—	36%
Present series (1938-1941)	75 (cleared)	52	55%

THE LYMPHATICS OF THE RECTUM—Our knowledge of the lymphatics of the rectum is based chiefly on the injection studies of Delamere, Poirier, and Cuneo,⁵ Villemin,⁶ and Rouvière.⁷ The intramural lymphatics which lie in the mucosa, submucosa, and muscle layers, are continuous with those in the rectosigmoid above and with the dermal and subcutaneous lymphatics of the anus below, and drain into the extramural lymphatic system This system consists of three main lymphatic trunks, the inferior, middle and superior, which correspond, in general, with the inferior, middle, and superior hemorrhoidal vessels, and constitute the three zones of spread—upward, lateral, and downward, described by Miles.^{1, 2}

The inferior trunks arise from the anal region in the lowest portion of the rectum, and drain, chiefly, to the inguinal nodes by way of the perineum and the inner side of the thigh, and probably, occasionally, directly to the iliac and sacral nodes in the pelvis The middle trunks arise in the rectum near the level of, and just above, the insertion of the levator ani muscles and pass laterally between the peritoneum and the levator muscles to the hypogastric and sacral nodes along the middle hemorrhoidal and sacral vessels The superior trunks arise from the entire length of the rectum from as low as the anal canal and drain into perirectal and mesocolic nodes along the superior hemorrhoidal and inferior mesenteric vessels As these three lymphatic trunks anastomose with each other, it is possible for a cancer of the rectum to have metastases along two or even three routes of spread

In none of our cases was extensive intramural lymphatic spread in the submucosa or muscularis found No attempt was made, however, to study this point by serial sections We are inclined to agree with Miles,¹ Wood and Wilkie,⁸ Westhues,⁹ Cole,¹⁰ and Monsarrat¹¹ that this type of spread is

rare As far as intramural extension is concerned it is probably safe to divide the bowel within a few centimeters of the tumor

UPWARD SPREAD—The extramural lymphatic spread in the 41 cases with lymph node metastases in our series of 75 rectal and rectosigmoid carcinoma, was studied carefully The main lymphatic path is upward along the superior hemorrhoidal vessels In over one-half of the cases with node metastases only three nodes or less were involved The largest number of

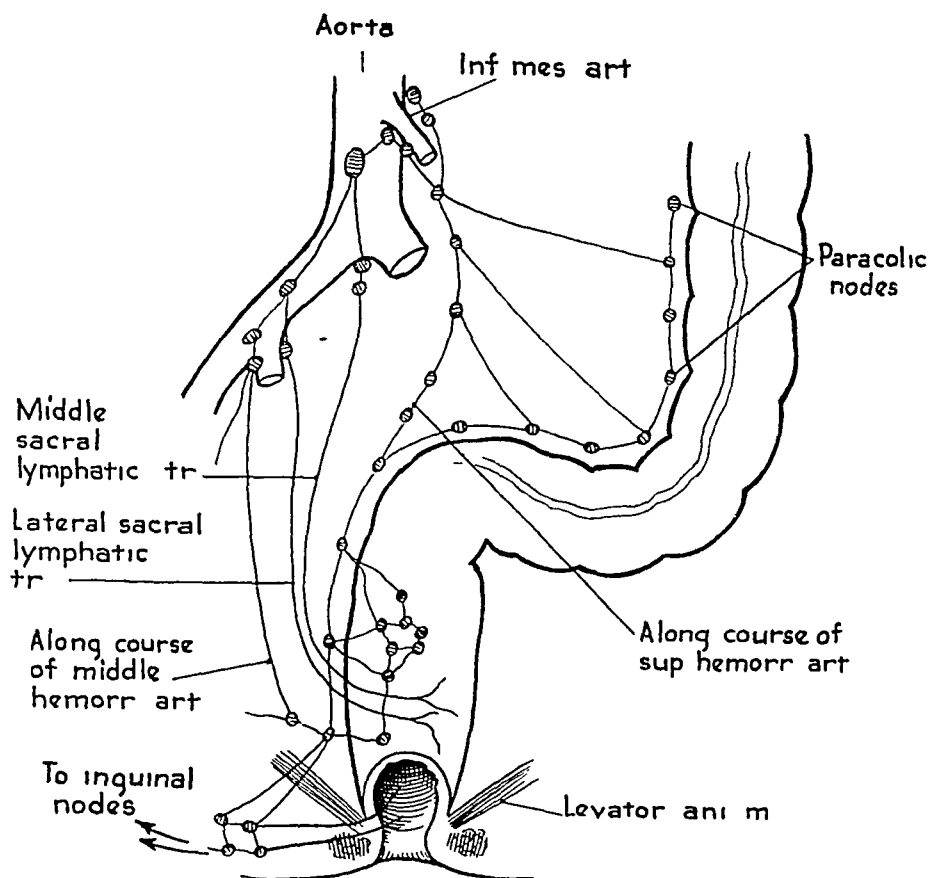


FIG 1—Schematic drawing of the extramural lymphatic system of the rectum and pelvic colon (after Miles and Villemain)

metastases in any one specimen was 13 In over one-half of these cases all the involved nodes lay within 3 cm of the tumor If cases without metastases are included, 73 per cent of all cases in this series were found to have either no metastases or very localized ones In the remaining 20 cases, or in nearly one-half of those with metastases, some of the involved nodes were at a considerable distance from the tumor One can conclude that the disease tends to remain localized and usually spreads slowly through the lymphatics but that exceptions to this rule are frequent

In nine, or 22 per cent, of the 41 cases with metastases the most proximal nodes near the point of division of the superior hemorrhoidal vessels showed metastases This group would be expected to have a particularly unfavorable prognosis Gabriel, Dukes, and Bussey¹² found that 30 per cent of their

cases with metastases were in this group. Five of our nine cases with the most proximal node involved, had had an abdominoperineal resection, and

TABLE II

NODE INVOLVEMENT IN 41 CASES WITH METASTASES

Cases with 1 node involved	11
Cases with 2 nodes involved	2
Cases with 3 nodes involved	10
	—
	23
Cases with 4 or more nodes involved	16
	—
	41

four had had a perineal excision. Thus, only 8 per cent of 62 cases having an abdominoperineal resection fell into this unfavorable group, whereas 40 per cent of our ten cases having a perineal excision were so classified. This emphasizes, strikingly, the inadequate removal of lymph node-bearing tissue obtained by the perineal operation.

In most of our cases the lymphatic spread of the disease progressed upward along the superior hemorrhoidal vessels in a fairly orderly manner. In seven of our 41 cases with metastases, however, the spread was definitely discontinuous, with a considerable gap of uninvolved nodes between the tumor and the more proximal involved ones. Figure 5 shows such a specimen. Gabriel, Dukes, and Bussey¹² had only one such case in 62 cases with metastases, whereas Wood and Wilkie⁸ reported six in 51 cases. This discontinuity of spread is undoubtedly explained by the fact that there

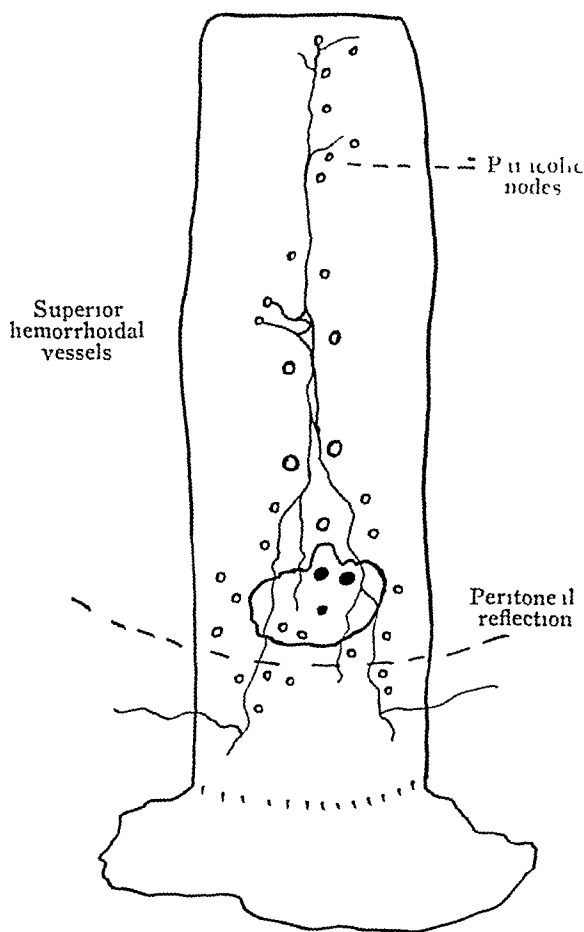


FIG. 2—A carcinoma with three metastatic nodes within three cm. of the tumor. For the sake of clarity not all uninvolved nodes are charted.
○ = nodes without metastases
● = nodes with metastases

are a variety of upward lymphatic pathways. In injection studies, Villemain, Montagne, and Huard⁶ describe three lymphatic routes passing upward with the superior hemorrhoidal vessels. The short paths are the most numerous and drain into a group of nodes near the bifurcation of these vessels. The middle paths pass upward without stopping at intermediate nodes to enter nodes

near the junction of the superior hemorrhoidal and lowest sigmoid vessels. The long paths pass upward without any intermediate stops to enter nodes near the junction of the left colic and the inferior mesenteric vessels. In six of our cases one or more nodes at the bifurcation of the superior hemorrhoidal vessels were involved, and in four cases nodes at the junction of the superior hemorrhoidal and lowest sigmoid arteries showed metastases. Two of these

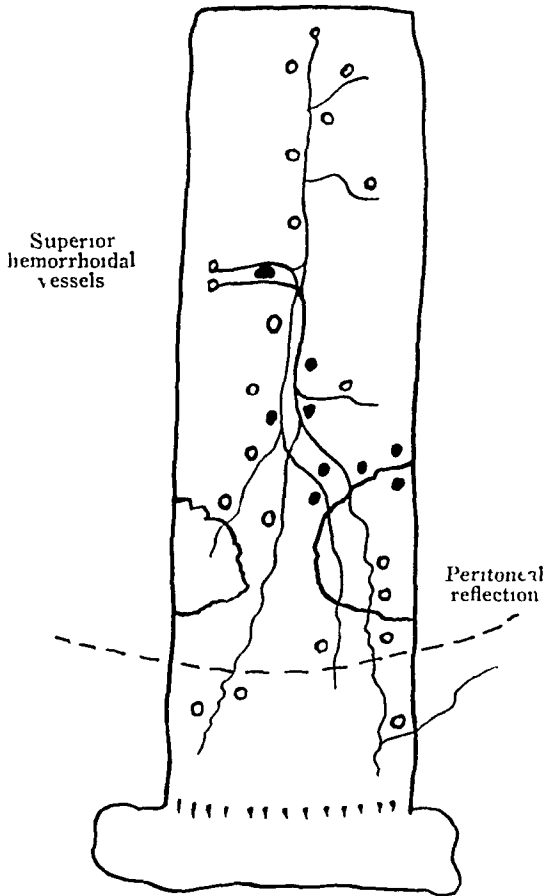


FIG. 3—A carcinoma removed by abdominoperineal resection with a metastasis in one of the most proximal nodes near the point of ligation of the superior hemorrhoidal vessels.

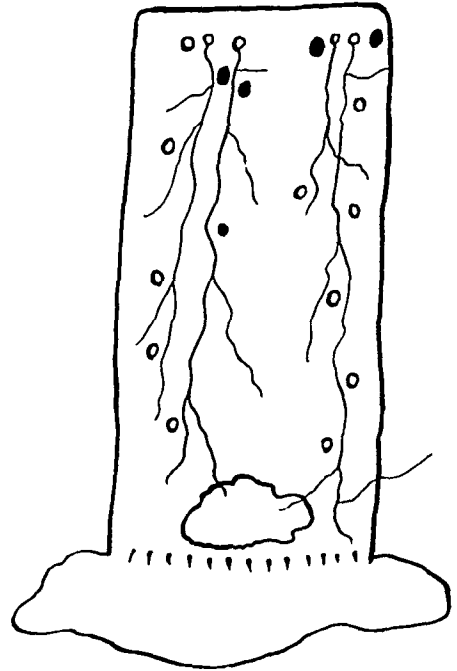


FIG. 4—A low rectal tumor removed by perineal excision with metastases in the most proximal nodes near the divided branches of the superior hemorrhoidal vessels.

four cases, apparently, represent examples of direct spread along the middle route. The other two showed metastases at both these sites, and may either represent spread by both the short and middle routes or a secondary relay from the short route which ends at the bifurcation. We had no cases illustrating metastasis by the long route, as the usual abdominoperineal resection does not extend as high as the origin of the left colic vessels.

The cases with lymph node metastases were also studied to compare the adequacy of simple perineal excision with that of abdominoperineal resection. The average limit of adequate removal of mesentery in the perineal operation was taken to be 3 to 4 cm above the peritoneal reflection. Only cases with tumors lying completely beneath the peritoneal reflection were taken. Some

cases with tumors partly above and partly below the peritoneum could probably have been included, but it was decided to limit the group only to cases best suited to the perineal operation. There were 17 cases with node metastases in this group. Only four of the 17 cases, or 24 per cent, appeared to be curable by perineal excision. In the remaining 13 cases, the involved nodes could not have been reached by such a limited operation. The inadequacy of this operation is obvious.

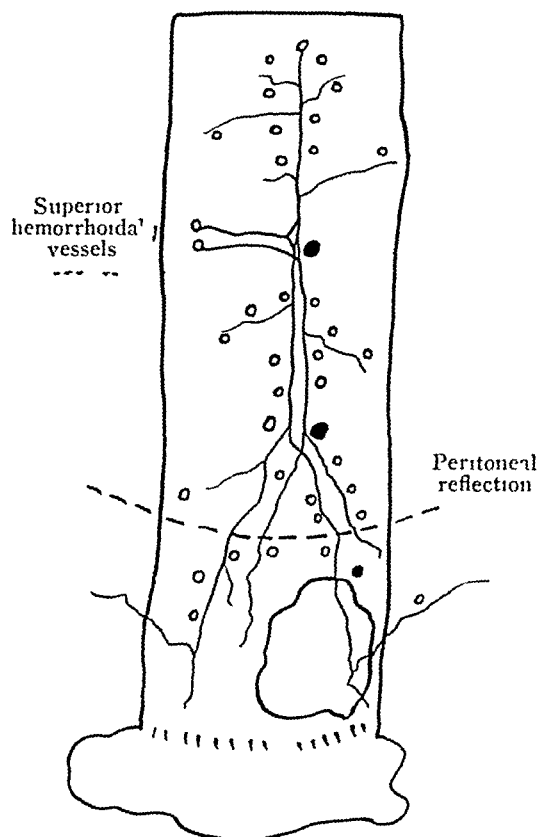


FIG 5—A carcinoma with discontinuous lymphatic spread. One involved node lies at the bifurcation of the superior hemorrhoidal vessels and another at their junction with the last sigmoid vessels.

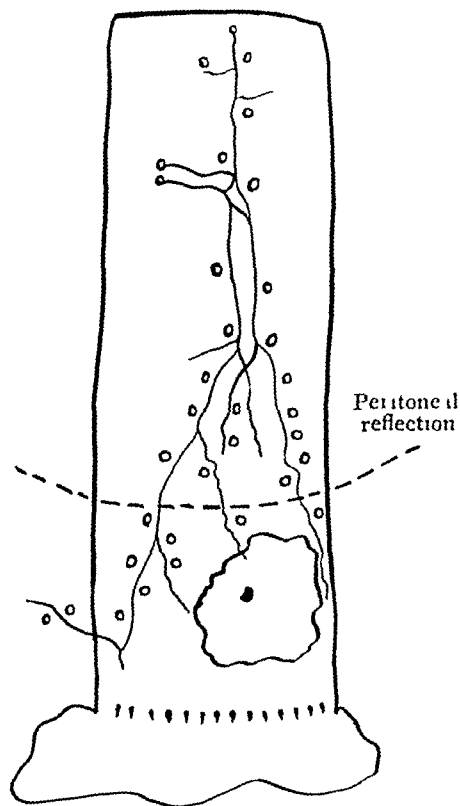


FIG 6—A low rectal carcinoma lying below the pelvic peritoneum. It has only one nearby metastasis and is suitable for the perineal excision operation.

LATERAL SPREAD—The lateral spread of the disease along the lymphatics accompanying the middle hemorrhoidal vessels has been an alternate route, emphasized especially by Miles^{1, 2} for carcinomata arising in the lower rectum near the level of the levator ani muscle insertion. Gilchrist and David had four cases, and Collier six, in their series. Wood and Wilkie had no instance of it. Our study showed only one case (Fig 8), which demonstrates upward, downward, and lateral spread from a tumor situated 6 cm above the pectinate line. It seems probable that lateral spread is most apt to occur in a low-lying tumor, where the main upward channels have been blocked by extensive metastases in the nodes. This was true in our case, and in Collier's six cases. As the middle hemorrhoidal vessels are sometimes hard to identify in cleared specimens it is possible that in one or two instances lymph nodes along this route may have been incorrectly charted along superior hemorrhoidal branches.

We agree with Gilchrist that section of the levator ani muscles should be made as widely as possible in order to reach nodes along this pathway. It seems probable, however, that this route of spread is of secondary importance, and occurs chiefly in advanced cases when the main upward path has been blocked.

DOWNWARD SPREAD—Downward lymphatic spread has also been emphasized, chiefly by Miles.^{1, 2} All writers on the subject agree that it occurs only when extensive metastases have occurred, blocking the other routes and causing retrograde lymph flow downward. Miles' observations were based mainly on cases with recurrent tumor nodules following inadequate perineal operations. We had only one case (Fig 8) which has already been cited as illustrating upward, lateral, and downward spread. In this case the tumor lay

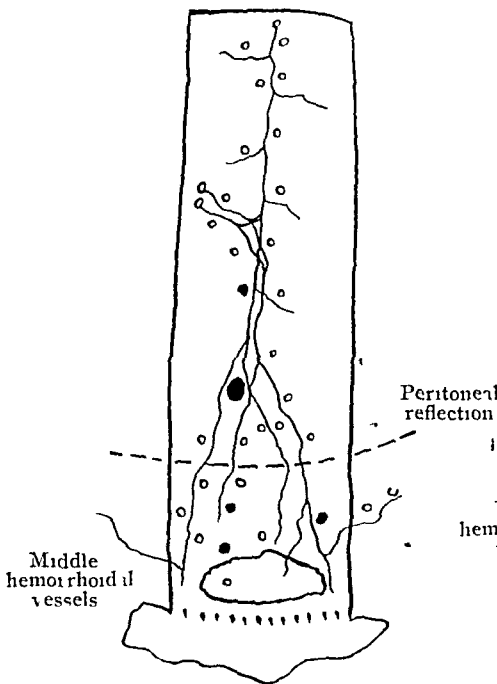


FIG 7—A low tumor with high node metastases unsuitable for the perineal excision operation.

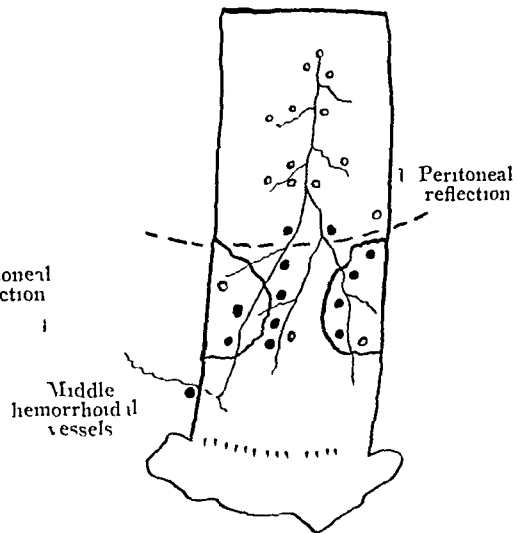


FIG 8—A low rectal carcinoma illustrating upward, lateral, and downward lymphatic spread. One involved node lies along the middle hemorrhoidal vessels two centimeters distal to the tumor. Thirteen of 46 nodes showed metastases.

6 cm above the pectinate line and had metastasized to 13 nodes, 12 involved nodes blocking the upward spread and one lying along the middle hemorrhoidal vessels, about 2 cm distal to the tumor. Westhues⁸ had only one case in 74 operative resections which lay 1 cm below the tumor and was associated with other metastases in the nodes above. Gilchrist reported one case with a metastasis 4 cm below the tumor, and Collier another, with the involved node lying 1 cm distal to the growth. It seems evident that downward lymphatic spread is of little importance except in advanced cases, which are probably already inoperable because of extension along the main lymphatic route upward. The very rare occurrence of downward extension in our

METASTASES OF CANCER OF RECTUM

cases, and in those of others, suggests that the operation of anterior resection with ligation of the superior hemorrhoidal vessels may have a greater usefulness for tumors just above the rectosigmoid junction. There were three of these cases in our series with metastases, and none showed evidence of retrograde extension

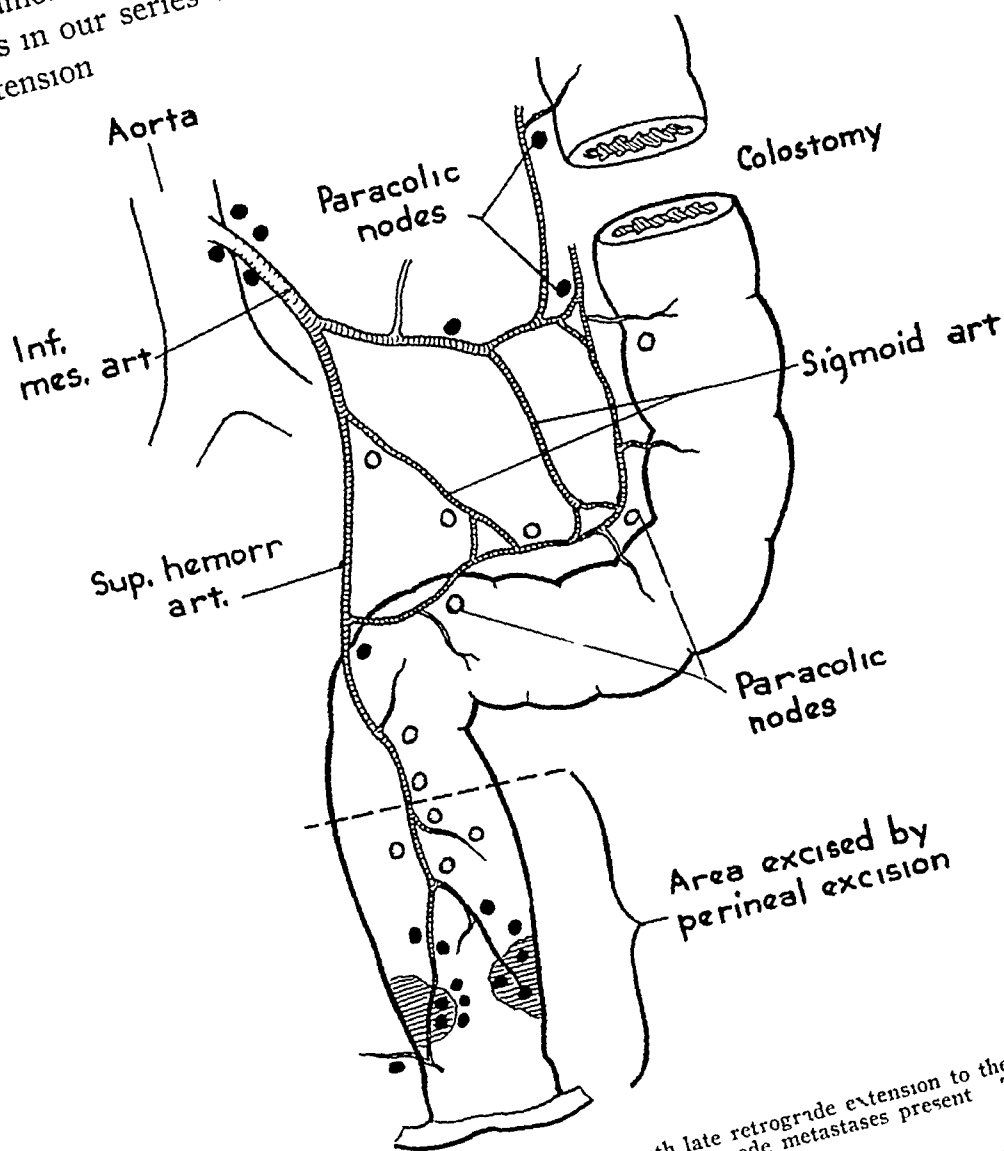


FIG 9.—A drawing of a tumor with late retrograde extension to the paracolic nodes following perineal excision and the probable node metastases present. This is the same case as that shown in Figure 8.

Metastases to the paracolic nodes are rarely found in operative specimens. There is, apparently, little tendency for retrograde flow to take place at this stage from the inferior mesenteric-superior hemorrhoidal chain laterally to the paracolic nodes along the pelvic colon. We found no instance of it in any of our 62 specimens removed by radical abdominoperineal resection. Miles^{1, 2} has stated that the paracolic nodes frequently show metastases by retrograde involvement. Wood and Wilkie³ had no cases of it. Gabriel, Dukes, and Bussey¹² had only one such case, and this was an advanced growth with extensive involvement of the higher nodes. We had one clinical example of it, very similar to one reported in detail by Miles. This case has already been

described (Fig 8) The patient, a female, age 55, with a low rectal tumor, had had a colostomy and a perineal excision performed in two stages At the first operation no liver or intraperitoneal metastases were found The tumor lay well below the peritoneal reflection One month later the perineal excision was performed, with removal of the lower 27 cm of the rectum Metastases were found in 13 of the 46 lymph nodes All the involved nodes were fairly close to the tumor Five months later, two recurrent tumor nodules were removed from both the proximal and distal limbs of the colostomy, and showed a histologic picture similar to that of the original tumor The nodules evidently represented retrograde spread from metastatic paracolic nodes It seems probable that involvement of the paracolic nodes occurs late, when radical surgery can offer little hope of cure

No relationship could be demonstrated between the size of the tumor and the frequency of metastases In fact the square area of bowel involvement was very slightly greater in the tumors without metastases than in those with them There was some correlation, however, between the amount of bowel circumference involved and the frequency of metastasis Thus, the incidence of node metastases was 53 per cent when the tumor was not completely annular, and 71 per cent when it was

VENOUS SPREAD

The occurrence of blood-borne metastases from carcinoma of the rectum has long been recognized, but the relative importance of this route of spread is still largely a matter of conjecture It is apparent from the frequency of five-year postoperative survivals in early cases without lymph node metastases, that venous metastasis does not usually precede lymphatic involvement Many surgeons, however, are familiar with the occasional small, early tumor, without node involvement, which is found to have liver metastases at operation Brown and Warren¹³ have recently thrown further light on this subject They studied a series of 165 cases of carcinoma of the rectum in which complete postmortem findings were available These were cases of patients dying immediately after resection or colostomy, survivals following operation, and cases dying of the disease without operation These cases were studied particularly for local blood vessel invasion in the tumor and for visceral and lymph node metastasis We have made a similar study in our series of 75 cases The search for vessel invasion by tumor cells was carried out as recommended by Brown and Warren At least three sections of the tumor were taken in each case and stained with Masson's aniline blue trichrome stain to emphasize the smooth muscle wall of the small veins The chief difficulty encountered was in differentiating tumor cells in veins from those in lymphatics The main point in differentiation was the presence of smooth muscle cells in the vessel wall not usually seen except in the largest lymphatics The finding of red blood cells in the lumen, especially if in considerable numbers, was also helpful Vessel invasion was found most frequently in the fat and connective tissue outside the muscle wall of the rectum along the deep

edge of the tumor. The next most common site was in the submucosa. Nearly every case was checked by Dr. A. P. Stout. Where there was any doubt of blood vessel invasion, it was not accepted.

BLOOD VESSEL INVASION—In the 75 specimens of carcinoma of the rectum in this series, in which blood vessel invasion was studied, definite invasion was found in 36 per cent. If 84 colon carcinomata, which were also studied, are added to this group, the incidence of vessel invasion rises to 41 per cent. Brown and Warren¹³ found it in 61 per cent, but the majority of their specimens were from autopsies of advanced cases in which

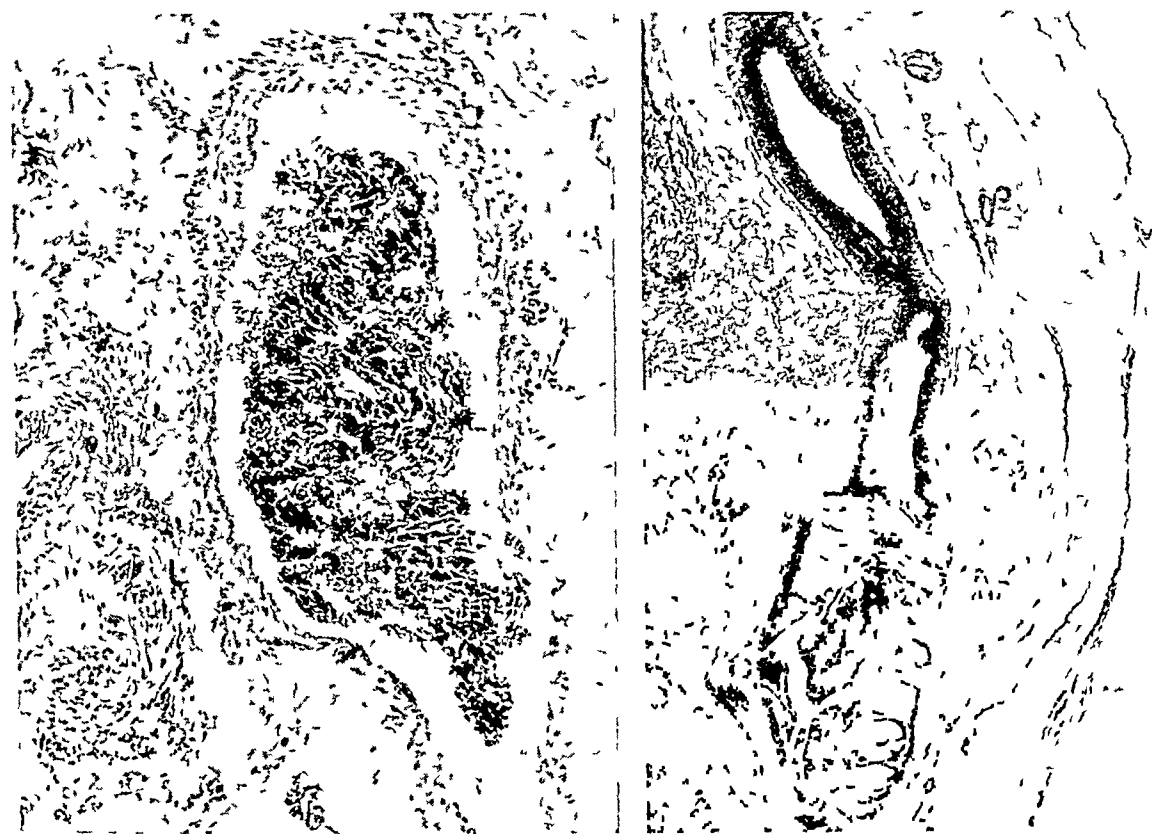


FIG. 10.—Tumor cells in a small vein accompanying artery (x125). Note the FIG. 11.—A tumor thrombus adherent to the wall of a vein (x28).

no operation had been attempted. A higher frequency of vessel invasion might be expected in these cases. They probably represent a less differentiated and more invasive group of tumors, and one in which vessel invasion has had more opportunity to occur in the late stages of the disease.

TABLE III
INCIDENCE OF LOCAL BLOOD VESSEL INVASION

	Total Cases	Vessel Invasion	
		Cases	Per Cent
Present series			
Rectum (operative specimens)	75	27	36%
Colon (operative specimens)	84	39	46%
Brown and Warren			
Rectum (operative and nonoperative specimens)	165	100	61%

The frequency of vessel invasion was found to vary with the degree of differentiation of the tumor. The growths were classified into three grades—I, II, and III, using as criteria the degree of invasive tendency, glandular arrangement, nuclear polarity, and the frequency of mitoses. This classification has been described previously¹⁵. Our series of 75 cleared specimens was increased by 15 other rectal carcinomata from a 1916-1932 group, which were also searched for tumor invasion in the veins. These additional cases had little effect on the result, but contributed to a larger series of cases. Twenty-five per cent of the Grade I cases had vessel invasion, 34 per cent of the Grade II cases, and all of the Grade III cases. That such a relationship should exist is not surprising. Just as poorly differentiated tumors frequently invade nerve sheaths, so do they often penetrate into the lumen of vessels. We have already shown previously¹⁵ the close relationship between the grade of the tumor, the frequency of node metastasis, and the five-year results. The value of grading is further demonstrated here. It influences prognosis, whether the disease spreads by the lymphatics or by the blood stream.

TABLE IV
VESSEL INVASION AND HISTOLOGIC GRADE

	Grade I	Grade II	Grade III
Vessel Invasion			
Absent			
Cases	12	38	0
Per cent	75%	66%	—
Present			
Cases	4	20	16
Per cent	25%	34%	100%

It was also found that the frequency of vessel invasion increased with the depth of penetration of the bowel wall by the tumor. The cases were grouped according to Dukes'¹⁴ classification. A-cases are those in which the growth is confined to the wall of the rectum, B-cases those which have penetrated to the extrarectal tissues but have not reached the lymph nodes,

TABLE V
VESSEL INVASION AND DUKES' CLASSIFICATION

	A	B	C
Vessel Invasion			
Absent			
Cases	11	20	19
Per cent	84%	69%	40%
Present			
Cases	2	9	29
Per cent	16%	31%	60%

and C-cases those which have metastasized to the regional nodes. Vessel invasion was found to be nearly four times as frequent in C-cases as in the A-cases, of which there were two. Presumably, the tumors which have penetrated farthest are usually the least differentiated and the most invasive.

They also have a greater opportunity for vessel invasion and a larger area available for its search. In addition to the two A-cases mentioned, vessel invasion was also found in a third case, a small, early carcinoma developing on a polyp. This was a very undifferentiated Grade III tumor, which was only excised locally, and was not included in this series of cleared specimens. This patient is still well, two years after operation.

VISCERAL METASTASES—Except in a few instances, it was not possible in this series to correlate the finding of blood vessel invasion with the later development of blood-borne metastases, because a sufficient follow-up period has not yet elapsed. Brown and Warren¹³ have shown in their cases that 67 per cent of those with local intravascular invasion had visceral metastases. They emphasize the fact that many tumor cells that enter the venous circulation fail to survive and grow in distant foci. The size of the vein involved is also an important factor, as Willis¹⁶ has pointed out. Large veins containing tumor cells are far more likely to have distant metastases than microscopic ones. In only seven of our cases had visceral metastases occurred at the time this report was made. However, 25 other cases of rectal carcinoma were found in an older series of cases,¹⁵ from 1916–1932, which had had definite visceral metastases, and whose specimens could be sectioned and searched for vessel invasion. All but three cases had liver metastases, with occasional lung and bone involvement as well. The presence of liver metastases was determined by autopsy findings, obvious metastases seen at operation or clinical evidence of a rapidly enlarging nodular liver.

There were 32 cases with visceral metastases in this combined group. When the distribution of these cases into three histologic grades was studied and compared to that of our recent cleared cases, a much larger percentage of Grade III cases was found in the former group. As we have already

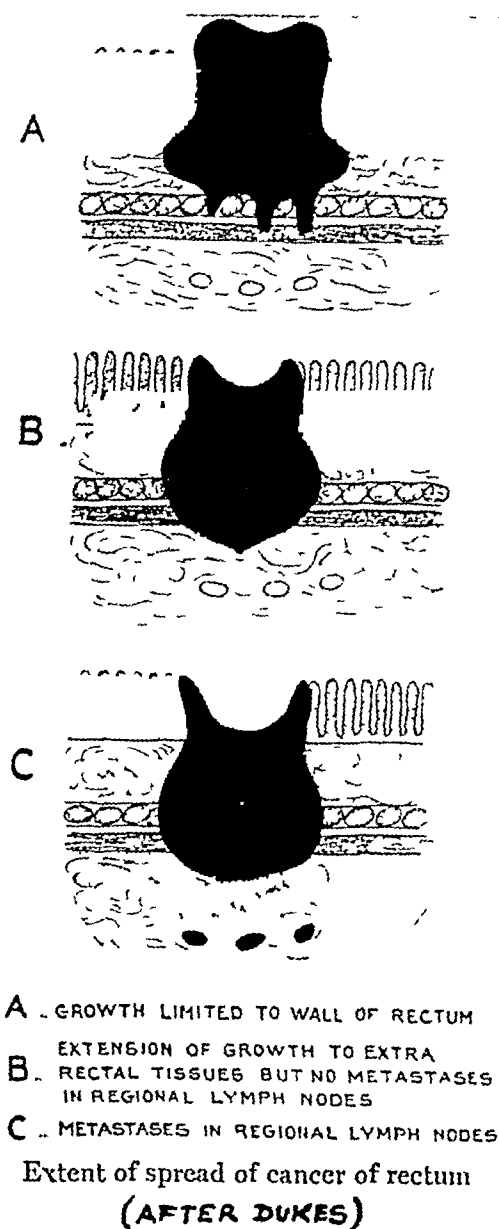


FIG. 12.—Dukes' classification of carcinoma of the rectum (after Dukes)

shown that vessel invasion is more frequent in Grade III cases, it is not surprising to find that visceral metastases are also more frequent

TABLE VI
DISTRIBUTION OF CASES BY HISTOLOGIC GRADE IN 32 CASES
WITH VISCERAL METASTASES AND IN PRESENT SERIES

	Grade I	Grade II	Grade III
Cases with visceral metastases selected from present and 1916-1932 series			
Cases	4	15	13
Per cent	13%	47%	40%
Present series (all cases)			
Cases	15	52	13
Per cent	19%	65%	16%

If this combined group with visceral metastases is analyzed as to bowel wall and node involvement, as measured by Dukes' classification, several striking facts appear. In the first place, no A-cases were found in this group. Evidently venous metastasis did not occur until after the tumor had completely penetrated the muscle wall of the rectum. Secondly, the percentage of B-cases, *i.e.*, cases with complete tumor penetration of the muscle wall, but without node involvement, with visceral metastases was surprisingly high and will be discussed further in the next paragraph. Finally, the proportion of C-cases, *i.e.*, cases with complete tumor penetration of muscle wall and node metastases, was found to be large, as might be expected. The comparison of this group with our recent cleared cases, and also with the 1916-1932 series, emphasizes these points. The farther the tumor penetrates the bowel wall the more frequent is vessel invasion and the chance of blood-borne metastasis. We have previously shown¹⁵ the close relationship between this classification and the five-year post-operative results. Here is another demonstration of its relation to prognosis.

TABLE VII
DISTRIBUTION OF CASES BY DUKES' CLASSIFICATION
IN 32 CASES WITH VISCERAL METASTASES
PRESENT SERIES AND 1916-1932 SERIES

	A	B	C
Cases with visceral metastases selected from present and 1916-1932 series			
Cases	0	8	24
Per cent	—	25%	75%
Present series (all cases)			
Cases	13	24	41
Per cent	17%	31%	52%
1916-1932 series ¹⁵			
Cases	20	49	40
Per cent	18%	45%	37%

Eight, or 25 per cent, of the 32 cases with visceral metastases were B-cases, and failed to show metastases in the regional nodes. Apparently blood-borne metastasis, before the nodes are involved, is not as rare as has been believed. In our 1916-1932 series the incidence of five-year

survivors after operation in the A-, B-, and C-cases was 100, 59, and 23 per cent, respectively. These results applied only to cases surviving operation five years and those dying of the disease. The fact that 100 per cent of the A-cases survived five years without disease, agrees with our findings that visceral metastases have not been found in the A-group. As for lymph node metastases, Dukes¹⁴ and Grinnell¹⁵ have shown that they almost never occur in the A-cases until the muscle layer of the bowel has been penetrated and the case can no longer be classed as an A-case. The difference between the survival rate of 100 and 59 per cent in the A- and B-cases can be largely explained by the greater liability of venous spread in B-cases, for as far as lymphatic spread is concerned all the A- and B-cases should have survived. It is possible, also, that some of the B-cases would have been classed as C-cases had the clearing technic been used in the search for node metastases. This would have raised the five-year survival rate of the B-cases somewhat nearer that of the A-cases.

TABLE VIII

FOLLOW-UP RESULTS ACCORDING TO DUKES CLASSIFICATION IN 1916-1932 SERIES
Cases Surviving Operation Five Years and Those Dying of Cancer in That Period

		A	B	C
Cases	63	10	27	26
Five-year survivors				
Cases	32	10	16	6
Per cent	51%	100%	59%	23%

When the cases with visceral metastases were studied for the presence of local vessel invasion, it was found to be present in nearly everyone. Out of the 30* specimens of rectal carcinoma removed at operation, vessel invasion was found microscopically in all but three, or 90 per cent. Brown and Warren were able to find it in all but one of their 70 cases with visceral metastases. In other words, the absence of vessel invasion after careful search in the sections from the primary growth will nearly always rule out the possibility of visceral metastases. Unfortunately, because of lack of sufficient follow-up period in our series, so far, the prognostic value of a positive finding of vessel invasion as regards visceral metastasis could not be determined. A negative finding, however, is probably far more important.

SUMMARY

(1) A series of 75 specimens of the rectum and rectosigmoid were cleared by the modified Spalteholz technic and studied for lymph node metastasis and blood vessel invasion.

(2) The average number of nodes per specimen was 52.

(3) Node metastases were found in 41 cases, or in 55 per cent. This incidence is 19 per cent higher than that found in a similar series of cases at this hospital, from 1916-1932 in which the clearing technic was not used.

(4) No intramural lymphatic spread of any significance was seen in any case.

* Two cases were omitted because sections were inadequate for vessel invasion study.

(5) The main extramural lymphatic spread is upward along the superior hemorrhoidal vessels. In over one-half of the cases with metastases, only three nodes or less were involved, and in over one-half of the cases the involved nodes lay within 3 cm of the tumor. In nine, or 22 per cent, of the cases with metastases the most proximal nodes, near the point of ligation of the superior hemorrhoidal vessels, were involved. Thus, 40 per cent of the ten cases having perineal excision, and only 8 per cent of the 62 cases having abdominoperineal resection, fell into this unfavorable group, with a probably inadequate operation.

(6) In most cases with node metastases the upward spread was relatively progressive and orderly. In 17 per cent, however, it was definitely discontinuous.

(7) Only four, or 24 per cent, of the 17 cases with node metastases, having tumors below the peritoneal reflection, could have had adequate node removal by perineal excision.

(8) There was only one proven case of lateral lymphatic spread along the middle hemorrhoidal vessels, and only one instance of downward spread found in our series.

(9) Metastasis to the paracolic nodes was not found in any of the specimens. One case showed clinical evidence of extension along this route following operation.

(10) The incidence of node metastasis was 18 per cent higher when the tumor was completely annular than when it was not. No relationship could be demonstrated between the square area of the tumor and the frequency of metastasis.

(11) Blood vessel invasion was found in 36 per cent of 75 specimens of carcinoma of the rectum, and in 41 per cent of a combined group of 162 colon and rectal tumors.

(12) The incidence of blood vessel invasion was four times as great in the Grade III cases as in the Grade I. It was present in all the Grade III cases. Cases with visceral metastases showed a higher incidence in Grade III than unselected cases.

(13) The incidence of visceral metastasis and its relation to local blood vessel invasion could not be determined because of the insufficient follow-up period.

(14) There were no A-cases with visceral metastases. Eight, or 25 per cent, of the 32 cases with visceral metastases were B-cases, without node involvement.

(15) Twenty-seven, or 90 per cent, of the 30 cases with visceral metastases showed blood vessel invasion. Only three cases, or 10 per cent, failed to show it.

CONCLUSIONS

(1) The use of the modified Spalteholz method for finding and charting lymph nodes will greatly increase the number of node metastases found, and will so aid in more accurate prognosis.

(2) The main extramural lymphatic spread is upward along the superior hemorrhoidal vessels. It tends to remain localized and to extend slowly in most cases. More distant spread, often discontinuous and unpredictable, is not uncommon, however.

(3) Lateral lymphatic spread along the middle hemorrhoidal vessels is probably infrequent and of secondary importance, occurring chiefly when the higher nodes are blocked by metastases.

(4) Downward lymphatic spread is exceedingly rare in operative specimens, and only occurs by retrograde flow when the high nodes are blocked.

(5) The rare occurrence of downward extension suggests that the operation of anterior abdominal resection, with ligation of the superior hemorrhoidal vessels, may have a wider field of usefulness for tumors near the rectosigmoid junction.

(6) Metastasis to the paracolic nodes is rare except in cases that are probably beyond operative cure.

(7) Perineal excision is a completely inadequate operation, even for carcinomata lying below the pelvic peritoneum.

(8) The tendency of rectal carcinoma to metastasize by way of the blood stream varies, in general, with the degree of differentiation of the tumor, and with the extent of local spread, as outlined by Dukes.

(9) Blood stream metastasis before the muscle wall of the rectum has been completely penetrated by the tumor is probably rare.

(10) Blood-borne metastasis after complete penetration of the muscle wall, but before the regional nodes are involved, is not as rare as has been believed.

(11) The value for prognosis of both the grading of tumors and their classification according to local spread has been further demonstrated.

(12) Failure to find local blood vessel invasion in the tumor after careful search is strong evidence that no visceral metastases exist.

REFERENCES

- ¹ Miles, W. E. *Cancer of Rectum*. London, Harrison and Sons, 1926.
- ² *Idem*. The Spread of Cancer of the Rectum. *Lancet* 208, 1218, 1925.
- ³ Gilchrist, R. K., and David, V. C. Lymphatic Spread of Carcinoma of the Rectum. *ANNALS OF SURGERY*, 108, 621, 1938.
- ⁴ Collier, F. A., Kay, E. B., and MacIntyre, R. S. Regional Lymphatic Metastasis of Carcinoma of the Rectum. *Surgery*, 8, 294, 1940.
- ⁵ Delamere, G., Poiriet, P., and Cuneo, B. *The Lymphatics*. Chicago, W. J. Keener and Co., 1904.
- ⁶ Villemain, F., Huard, P., and Montagne, M. Recherches anatomiques sur les lymphatiques du Rectum et de l'Anus. *Rev. de Chir.*, 63, 39, 1925.
- ⁷ Rouviere, H. *Anatomy of the Human Lymphatic System*. Paris, Masson et Cie, 1932. Translated by Tobias, M. J., Ann Arbor, Michigan, Edwards Brothers, Inc., 1938.
- ⁸ Wood, W. Q., and Wilkie, D. P. D. Carcinoma of the Rectum. An Anatomico-Pathological Study. *Edinburgh Med. Jour.*, 40, 321, 1933.
- ⁹ Westhues, H. Die pathologisch-anatomischen Grundlagen der Chirurgie des Rektumkarzinoms. Leipzig, Georg Thieme, 1934.

- ¹⁰ Cole, P P The Intramural Spread of Rectal Carcinoma Brit Med Jour, 1, 431, 1913
- ¹¹ Monsarrat, K W, and Williams, I J Intramural Extension in Rectal Carcinoma Brit Jour Surg, 1, 173, 1913-1914
- ¹² Gabriel, W B, Dukes, C, and Bussey, N J R Lymphatic Spread in Cancer of the Rectum Brit Jour Surg, 23, 395, 1935
- ¹³ Brown, C E, and Warren, S Visceral Metastasis from Rectal Carcinoma Surg, Gynec, and Obstet, 66, 611, 1938
- ¹⁴ Dukes, C The Classification of Cancer of the Rectum Jour Path and Bacteriol, 35, 323, 1932
- ¹⁵ Grinnell, R S The Grading and Prognosis of Carcinoma of the Colon and Rectum ANNALS OF SURGERY, 109, 500 1939
- ¹⁶ Willis, R A The Spread of Tumours in the Human Body London, J and A Churchill, 1934

PRIMARY ABSCESS OF THE LIVER DUE TO ANAEROBIC NONHEMOLYTIC STREPTOCOCCUS

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ABSCESSSES OF THE LIVER may be classified into two main groups (a) Amoebic, which are usually single and which are associated with amoebic dysentery, and (b) pyogenic. The latter group may be due to invasion by a variety of organisms, and as noted by Ochsner,⁶ may (1) follow infection in areas drained by the portal system, e g, appendix, rectum and other portions of the bowel, (2) spread from contiguous structures, e g, cholecystitis, gastric and duodenal ulceration, subphrenic space infection, (3) result from trauma by penetration from without or by infection in a hematoma with organisms already present in the liver, and (4) blood-borne infections *via* the hepatic arteries. In many instances no antecedent causal infection is demonstrable.

Although much has been written on the subject of pyogenic abscess of the liver, its bacteriology has not been emphasized. In a large series of collected cases, Ochsner⁶ was able to find only 184 in which the bacteriology of the pus was reported. In these *B coli*, streptococci and staphylococci predominated. Failure to include the results of anaerobic cultures in many instances throws some doubt on the validity of the assumption that the above aerobes were the only organisms present. With the gastro-intestinal tract teeming with anaerobic bacteria, it does not seem as if they would be consistently absent from abscess of the liver. As future series of cases are reported, in which careful anaerobic as well as aerobic cultures are made other organisms may be included as being etiologic. It is to be expected that anaerobes will be isolated more frequently.

We have had the opportunity recently to study a case where precise bacteriologic examination demonstrated the complete absence of the usual aerobic organisms isolated in abscess of the liver, and the exclusive presence of a strictly anaerobic nonhemolytic streptococcus. Three points in this case are of particular interest.

- 1 The presence of, and to our knowledge, for the first time recorded a primary solitary hepatic abscess from which a pure culture of an anaerobic nonhemolytic streptococcus was recovered.

- 2 The unknown portal of entry of the organisms.

- 3 The inconstancy of the symptoms and clinical findings.

In 1893, Veillon,¹⁰ described under the name of *M foetidus*, a strictly anaerobic coccus, growing in short chains, and producing gas and a fetid odor in cultures, which he isolated from cases of Ludwig's angina, perinephric abscess and suppurative Bartholinitis. In 1895, Kronig,¹ and Menge,⁴ independently described a strictly anaerobic streptococcus which they found in the vagina in pregnancy, and later, in collaboration,⁵ isolated several strains from the vagina and lochia in infected puerperal cases as well as from parametrial suppurations and peritonitis. Their organism was called *Streptococcus anaerobius*. Lewkowicz² (1901) isolated from the mouths of sucklings, a third variety of an extremely minute streptococcus growing only under strictly anaerobic conditions (*Streptococcus mucros*).

The importance of these organisms in relationship to puerperal septicemia was first insisted on by Schottmuller⁹ (1910), although their presence in the genital tract in the puerperium had been noted by several earlier workers.⁸ Schottmuller's observations have been extended and confirmed by many other workers.⁸ It would seem that the anaerobic streptococci form part of the flora of the normal genital tract.⁸

In recent years, numerous other reports have appeared in the literature describing the pathogenicity of anaerobic streptococci for man.⁸ Dental infections harbor these organisms. They have been grown in pure or mixed cultures derived from chronic otitis media, cerebral abscess, meningitis and frontal sinusitis. Many believe that they are responsible for the severe infections following "human bites." Ulcerating carcinomata connected with the oral cavity frequently yield an aerobic streptococci on culture. They have been found in the blood in some cases of postanginal sepsis and bacterial endocarditis. They have been isolated repeatedly from abscesses of the lung and putrid empyemata. They have been cultured from the alimentary tract, including the gallbladder, and from exudates associated with appendicitis. Anaerobic streptococci in association with *B coli* are said to cause the foul odor of peritonitis and appendiceal abscess, which is attributed popularly and erroneously to the colon bacillus alone. Bacterial synergistic gangrene of the abdominal or chest wall which sometimes follows operations on the gastrointestinal tract or pleural cavity has been found by Meleney⁸ to be due to the symbiotic action of staphylococci and micro-aerophilic nonhemolytic streptococci. Urinary and genital tract infections due to anaerobic streptococci have been reported, and they have been recovered from traumatic wounds both civil and military.

As far as we can determine, only one case of abscess of the liver from which anaerobic streptococci were cultured is on record. McDonald, Henthorne and Thompson³ reported a case of perforated duodenal ulcer, repaired surgically. Two and one-half months later, at necropsy, a huge subdiaphragmatic abscess was found, and also multiple chronic abscesses of the liver. The duodenal ulcer was entirely healed. Anaerobic nonhemolytic streptococci, in pure culture, were grown from the abscesses of the liver.

Case Report—A D, white, male, age 19, was admitted to Harkness Pavilion of the Columbia Presbyterian Medical Center, April 14, 1941, complaining of chills and fever of four weeks' duration. On March 19, 1941, two days after playing football in the snow, he felt chilly, and was admitted to the college infirmary. The following day he had a shaking chill and on subsequent days, had two other severe chills. There was persistent fever varying from 98.6° to 104.4° F, usually reaching a peak at 8 P. M. The patient awakened almost every day about 5:30 A. M. with a drenching sweat. He suffered from anorexia, with concomitant weight loss. During the first four weeks of his illness, he had a mild unproductive cough. About April 2, 1941, two weeks after the onset of the illness, he noticed a slight, inconstant pain in the right upper quadrant of the abdomen below the costal margin, which "caught" him when he breathed. This pain was present for two days and then subsided only to recur six days later. During the latter episode he complained also of constant pain in his right shoulder, made worse by deep inspiration. The shoulder was not tender nor was it hot or swollen. There was no history of diarrhea or of jaundice. There had been no known exposure to enteric disease. He had spent part of the preceding summer in Mexico, but otherwise had not been out of the United States. He had taken no unpasteurized milk. He had noted a small pustule on the back of the neck several months before the onset of his illness, which subsided without drainage. There was no history of familial disease.

The past history included (1) pneumonia in 1930, complicated by bilateral otitis media, (2) serum sickness in 1930, following tetanus antitoxin, and (3) uncomplicated measles in 1934. Operations included several partial tonsillectomies, the last in 1930, as well as myringotomies in 1930 and 1933. He had been exposed to tuberculosis in April, 1940, by a maid in the household who had contracted pulmonary tuberculosis. Physical examination at the time of college entrance in September, 1940, revealed a well-developed young man, weighing 165 pounds, with no pathologic findings other than slight dental caries. Dental roentgenograms in December, 1940, showed no abscesses.

The reports of the laboratory data which were brought in with the patient were as follows. Hemoglobin ranged from 12.2 gm (84 per cent) to 13.5 gm (93 per cent), R.B.C. from 4,010,000 to 4,270,000, the W.B.C. from 10,000 to 17,000, and the polymorphonuclears from 72 to 85 per cent. There was no eosinophilia, and there was a marked increase in the number of young polymorphonuclears. Urinalyses showed normal findings repeatedly. A single urine culture revealed *B. coli* and *Staphylococcus albus*. Three blood cultures showed no growth. Five stool cultures yielded no enteric pathogens. Blood agglutination tests were negative for *B. typhosus* O and H antigens, *B. paratyphosus*, A, B, and C, *B. abortus* and *melitensis*, *B. proteus* X 19, and for the Forssman antigen. Roentgenologic examinations of the chest, spine, and tibiae were negative.

No definite diagnosis had been made. Therapy had included courses of sulfathiazole, quinine bisulfate, and sodium salicylate. These were ineffective. Because no improvement took place the patient was transferred to the Harkness Pavilion, 26 days after the onset of the illness.

Physical examination, on admission, revealed a well-developed, but thin, chronically and acutely ill young white male, who showed obvious weight loss and pallor, and no jaundice or petechiae. Temperature 104° F, pulse 110, respirations 24, and blood pressure was 135/85. The right tympanic membrane was scarred. There were a few shotty posterior cervical lymph nodes. Examination of the thorax revealed inconstant tenderness over the 7th, 8th and 9th ribs on the right, and 9th, 10th and 11th ribs on the left. This tenderness was more marked on the right side. Examination of the lungs disclosed a short, inconstant friction rub over the 7th and 8th ribs anteriorly on the right side. At times, on deep inspiration, the patient grimaced with pain and at these times the right chest expanded less than the left. Abdominal examination showed right upper quadrant tenderness and slight spasm. However, there was no costovertebral angle tenderness and the liver and spleen were not palpable. By percussion the liver dullness

extended from the right 5th rib to the costal margin. An interesting observation on subsequent examinations was the production of pain in the right shoulder with deep inspiration with the patient supine. This phenomenon could not be reproduced with the patient in the sitting position.

Repetition of the blood counts, blood agglutination tests, urinalyses and stool examinations yielded essentially the same results as those made prior to admission. Three blood cultures showed no growth after incubation under aerobic, anaerobic and CO₂ conditions.

The blood chemistry findings are shown in Table I.

TABLL I
BLOOD CHEMISTRY DATA

	4/16/41 Admission	4/26/41 Preoper	5/10/41 Postoper	6/25/41 Before Discharge
Serum inorganic phosphorus	4.7 mg %	4.6 mg %		4.2 mg %
Serum phosphatase	12.1 Bodansky U	11.8 Bodansky U		4.6 Bodansky U
Serum bilirubin	Very faint trace	0.8 mg %		
N P N	21 mg %	38 mg %		29 mg %
Serum cholesterol	95 mg %	113 mg %	155 mg %	167 mg %
Free		43 mg %	52 mg %	
Ester		70 mg %	103 mg %	
Serum protein	6.7 mg %	7.5 mg %		7.3 mg %
Albumin	3.6 mg %	3.7 mg %		4.5 mg %
Globulin	1.1 mg %	3.8 mg %		2.8 mg %
Euglobulin		0.9 mg %		
Cephalin flocculation test			±	
Bromsulphthalein test for liver function				5% retention of dye after 30 minutes

Additional studies included a plain film of the abdomen, which showed normal kidney, ureter and bladder shadows, but an indistinct right psoas shadow, the liver shadow was not enlarged and its lower margin was normal. Six chest films and fluoroscopic examinations showed normal diaphragmatic contours. However, there was a diminished excursion of both domes of the diaphragm and the right dome was consistently less mobile than the left. There was evidence of thickening of the right diaphragmatic pleura and a small amount of free pleural fluid was noted at the right lung base, but this latter finding was not constant.

Course—The patient was studied for 18 days, during which time he received two whole-blood transfusions. He suffered repeated chills of varying intensity and the spiking temperature, ranging from 100.2° to 105.4° F, continued, as did the weakness, anorexia, and sweats. An otolaryngologist was unable to demonstrate any focus of infection in the ears, nose, throat or paranasal sinuses.

Because of the chills and spiking temperature, the vague pains in the right lower chest and right upper abdomen, the continued prostration of the patient, the leukocytosis, the disturbed blood chemistry, and the fluoroscopic finding of a consistently diminished excursion of the right diaphragm, a clinical diagnosis was made of a purulent infection near the right diaphragm, probably intrahepatic. The signs of right pleural irritation were thought to be secondary. Solitary amoebic abscess of the liver was regarded as a possibility, and a course of emetine hydrochloride was given, but with no effect. Accordingly, surgical exploration of the right upper quadrant of the abdomen was deemed advisable.

Operation—May 2, 1941 (19 days after admission, and 45 days after the onset of the disease). Exploratory celiotomy was performed through a right paracostal incision. On opening the abdomen it was found that the liver was much larger than had been appreciated preoperatively, and extended 4–5 cm below the costal margin. On the superior surface of the right hepatic lobe, an area of induration, 9 cm in its greatest diameter, was felt. The dome of this indurated area felt softer than the surrounding

liver There were numerous delicate adhesions between the liver and the diaphragmatic peritoneum There was no pus in the subphrenic space There was no evidence of infection in the right perinephric region, in the right lumbar gutter, or in the subhepatic region The appendix appeared normal A diagnosis of a deeply situated abscess of the right lobe of the liver was made

The right 9th rib was resected directly over the suspected area on the superior surface of the liver The pleura was incised and immediately sutured to the diaphragm The diaphragm was then incised exposing the liver Two strips of iodoform gauze packing were placed between the diaphragmatic peritoneum and the surface of the liver The transpleural wound was packed with vaselined gauze The abdominal incision was closed without drainage Forty-eight hours later the packing was removed from the transpleural wound and a small suction trochar was introduced into the soft spot in the liver At a depth of 3.5 cm from the surface, 60 cc of yellow-brown pus was encountered The tract was enlarged with the electrocoagulator, without bleeding A soft rubber catheter drain was placed into the cavity, and the wound was packed

Course—A transfusion was given during the first operation and another four days after the second operation Examination of the pus showed the presence of minute gram-positive cocci in chains, but no amoebae nor other parasites No chemotherapy was carried out The postoperative course was uneventful The white blood cells fell progressively to 7,600, with 53 per cent polymorphonuclears Hemoglobin and red blood cells remained at normal levels From the first day after the second-stage operation the temperature remained below 101° F, and the temperature, pulse and respirations were normal from the 20th postoperative day The abdominal wound healed *per primam* There was profuse drainage from the abscess for 20 to 25 days, with gradual subsidence The patient was allowed up on the 44th postoperative day, and was discharged on June 26, 1941, 54 days after operation, in excellent condition, weighing 159 pounds, or six pounds under his average weight He has remained well When seen six months later he weighed 175 pounds, and had been attending college for two months

Bacteriology—Gram stain of the exudate showed the presence of many pus cells and a small number of minute gram-positive cocci in chains Repeated examinations of fresh specimens failed to reveal the presence of amoebae, giardia, or other parasites All dark field examinations were negative Aerobic 5 per cent sheep's blood agar plates gave no growth Anaerobically however, there was growth in dextrose meat broth and on the blood agar plates Smears from the broth showed the same gram-positive cocci seen on direct smear of the exudate The blood agar plates yielded a pure culture of the same organism The biochemical reactions of this organism corresponded to those of the *Streptococcus intermedius*, of Prevot⁷ The organisms remained strict anaerobes on repeated subculture Subsequent cultures of the pus also grew out this anaerobic nonhemolytic streptococcus

SUMMARY

1 This is the first report, as far as the authors have been able to determine, of a primary, solitary abscess of the liver from which a pure culture of an anaerobic nonhemolytic streptococcus was recovered Careful examinations revealed no apparent portal of entry of the organisms

2 A brief review of the literature on the pathogenesis of the anaerobic nonhemolytic streptococci is presented

3 The inconstancy of the symptoms and localizing signs in this case are significant

4 Pain in the shoulder with deep inspiration in the supine position and its absence in the sitting position are offered as a contributory sign in the diagnosis of abscess of the liver

5 The importance of routine anaerobic as well as aerobic cultures is emphasized by this case

REFERENCES

- ¹ Kronig Über die Natur der Scheidenkeime, Specille über das Vorkommen Anaerober Streptokokken im Scheidensekret Schwangerer Zbl f Gynak, 19, 409-412, 1895
- ² Lewkowicz, X, Recherches sur la flore microbienne de la bouche des nourrissons Arch de Med Exper, 13, 633-60, 1901
- ³ McDonald, J R, Henthorne, J C, and Thompson, L Rôle of Anaerobic Streptococci in Human Infections Arch Path, 23, 230-240, 1937
- ⁴ Menge, K Berichte aus gynakol Gessellschaften u Krankenhausern Zbl f Gynak, 19, 433, 1895
- ⁵ Menge, K, and Kronig Über verschiedene Streptokokkenarten Monatschr, f Geburts u Gynak, 9, 703-737, 1899
- ⁶ Ochsner, A, DeBakey, M, and Murray, S Pyogenic Abscess of the Liver Am Jour Surg, 40, 292-319, 1938
- ⁷ Prevot, A R Manuel de classification et de Determination des Bacteries Anaerobies Paris, 1940, Masson & Cie
- ⁸ Sandusky, Wm R, Pulaski, E J, Johnson, B A, and Meleney, F L The Anaerobic Nonhemolytic Streptococci in Surgical Infections on a General Surgical Service Presentation of cases and review of literature Surg Gynec & Obst, in press
- ⁹ Schottmuller, H Zur Bedeutung unserer Anaeroben in der Pathologie, insbesondere bei puerperalen Erkrankungen, (Streptococcus putridus, Bac phlegm-empysemat, Bac tetani) Mitt ad Grenzgeb d Med u chir, 21, 450-490, 1910
- ¹⁰ Veillon, M A Sur un microcoque anaerobie trouve dans des suppurations fetides Soc de Biol, Compt Rendus, 45, 807-9, 1893

SEVERE TRAUMA TO THE LIVER WITH "HEPATORENAL SYNDROME"

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THE CLINICAL IMPORTANCE of hepatic failure as a cause of collapse in certain cases following operation upon the biliary tract was first emphasized by Heyd (1924). Since then a number of clinical and experimental articles on "liver death" and "liver-kidney failure" have appeared. The papers of Boyce, Helwig, and associates, and Wilensky, are particularly valuable for their discussions of this somewhat controversial subject. Fuitwaengler (1927) is said to have been the first observer to report a case in which the possible relation between trauma to the liver and the subsequent development of damage to the kidney was recognized. Recently, Orr and Helwig (1939) directed attention to the importance of the recognition of the "hepatorenal syndrome" in certain cases of severe trauma to the liver. Boyce's monograph (1941) offers an excellent review of the subject of hepatic insufficiency.

The following case demonstrates some interesting clinical, physiologic, and biochemical observations made on a healthy young adult patient who received an injury limited to the liver.

Case Report—A male, age 20, was injured in an automobile accident, September 3, 1940. The lower thoracic and upper abdominal regions were crushed between the engine and the front seat of the car. Fifteen minutes after the accident he was brought to the hospital in profound shock—pale, cold, and restless—but conscious and complaining of abdominal pain. Temperature 98° F, pulse 120, blood pressure 40/20. There were lacerations and abrasions about the face and mouth. Generalized guarding and tenderness were present throughout the abdomen, most marked in the right upper quadrant. Peristaltic activity was diminished. Treatment for shock included an intravenous infusion of 1000 cc of glucose solution, and a transfusion of 500 cc of citrated whole blood. After six hours of observation his condition had improved and the blood pressure was 114/70. The abdominal pain and signs of peritoneal irritation had increased. The pulse rate remained about 128, but was considerably improved in quality. At that time, the hemoglobin content of the blood was 120 per cent, the red blood cell count 565 million, and the white count 53,000. About six hours after the patient had sustained the injury, abdominal exploration was undertaken under ether anesthesia. Another transfusion of citrated whole blood was given during the operation. A deep laceration, about 10 cm in length, was felt in the dome of the right lobe of the liver. It was bleeding freely and the abdomen was filled with blood, 1500 cc of blood was aspirated from the abdominal cavity, but autotransfusion was not performed as the blood contained bile. The laceration in the liver was inaccessible for suturing, and a large, hot, moist pack was inserted into the defect, while the remainder of the abdomen was explored, but no further injury was found. The pack was removed and the bleeding

had ceased. A Penrose drain was placed to the laceration in the liver and brought out through a small separate wound in the right lateral subcostal region. The abdomen was then closed. The operation lasted 53 minutes and was tolerated fairly well. The patient reacted from his anesthetic in the usual length of time. His pulse and blood pressure were within normal limits for several hours, and during this early postoperative period he voided a total of 240 cc of normal urine. Shortly after the operation, the temperature was 103.4° F, and it remained at about this level until the next day. On the morning after the operation the patient appeared weak, the pulse was very rapid and of poor volume (uncountable), and the blood pressure had fallen to 88/55. That afternoon he became wildly delirious and the temperature rose to a maximum reading of 107.8° F rectally, the extremities were cold and cyanotic, the pulse was barely discernible, and the systolic blood pressure varied from 70 to 80. The abdomen remained flat, soft, and without tenderness. There was no urinary output for 19 hours, and catheterization yielded only 50 cc of dark urine containing a trace of albumin and an occasional cast. The non-protein nitrogen in the blood was elevated to 110 mg per 100 cc of blood. Parenteral fluids, glucose and physiologic saline were given and continuous oxygen inhalation therapy was provided. Three transfusions each consisting of 500 cc of citrated whole blood, were given over a period of several hours. Sedation was accomplished with paraldehyde. Following the first of these transfusions the blood pressure was increased to 100/80, and the urinary output gradually began to increase. The temperature declined to 103° F, and remained around this level for the subsequent three days and then gradually became normal. He was comatose and restless during the first two days of the reaction and then rather suddenly became mentally clear. The abdomen remained soft and non-tender throughout the entire postoperative period. There was no further hypotension or oliguria and the azotemia decreased rapidly. A few red blood cells appeared in the urine on the second day after operation and such cells were found thereafter for several days. Albuminuria was present for six or seven days and then disappeared. Tests of the liver and kidney function by excretion of dye were not performed until the fifth postoperative day and at

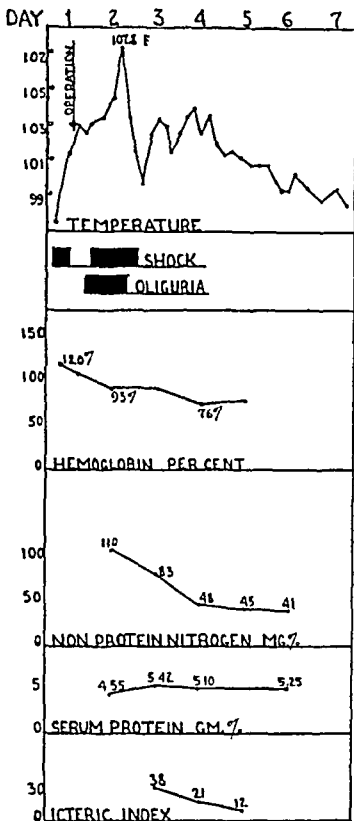


CHART I

that time they were within normal limits. Mild clinical icterus developed and the icteric index was 38 units on the third day following the injury, 21 on the fourth postoperative day and 12 on the fifth day. The prothrombin time was estimated as 80 per cent of normal on the third day and 100 per cent on the fifth. During the first day a considerable amount of bile-tinged serous fluid soaked the dressings covering the drainage wound, and a moderate amount of clear bile drained for several days thereafter. There was no evidence of bleeding from the drainage wound at any time after the operation. After a stormy course during the first four days, the patient made a good recovery. He was discharged from the hospital, October 7, 1940, and has remained well. Chart I and Table I show the more important laboratory determinations that were made during the critical part of his illness. The severity of the illness, and the urgent need for active treatment necessarily limited the laboratory studies.*

* The biochemical determinations were done by Mrs. Ruth Nelson Cornell in the laboratory of Dr. Raymond Reitzel.

TABLE I

LABORATORY DATA IN THE CASE OF A PATIENT WITH SEVERE LIVER TRAUMA WHO DEVELOPED COLLAPSE WITH VERY HIGH TEMPERATURE AND OLIGURIA ON THE DAY FOLLOWING HIS INJURY. THE LIST INCLUDES THOSE EXAMINATIONS THAT WERE MADE DURING THE FIRST SIX DAYS.

Blood	Date	9-3-40	9-4-40	9-5-40	9-6-40	9-7-40	9-8-40
Hemoglobin (145 g = 100%)		120%	93%	93%	76%	79%	—
Erythrocytes (millions per cu mm)		5.65	—	4.30	3.90	4.60	—
Leukocytes (number per cu mm)		53000	19000	14000	10000	19000	—
Urine							
Specific gravity		QNS	1.022	1.027	1.028	1.026	—
Albumin		—	Trace	Trace	Trace	Trace	—
Cast		—	Few	Few	Few	Few	—
Red blood cells (per hpf)		0	0	2	5	50	10
Urobilin (Schlesinger's test)		—	—	0.110	+ 1.1	+ 1.40	—
Bile		—	0	0	0	0	—
Blood Chemistry							
Nonprotein nitrogen (mg %)		—	110	83	48	45	41
Creatinine (mg %)		—	—	2.6	—	2.9	—
Plasma chlorides (mg %)		—	663	679	—	—	623
Serum protein (Gm %)		—	4.55	5.42	5.10	—	5.25
Serum albumin (Gm %)		—	3.56	4.36	4.20	—	3.62
Serum globulin (Gm %)		—	0.99	1.06	0.90	—	1.63
Icterus index (units)		—	—	38	—	21	12
Glucose (mg %)		—	—	112	—	—	—
Plasma cholesterol (mg %)		—	—	159	—	—	—
Prothrombin time (H. P. Smith method)		—	—	—	80%	—	100%
Rose bengal (retention in serum) 8 minutes		—	—	—	—	—	63%
(liver function test) 16 minutes		—	—	—	—	—	43%
Phenolsulfonphthalein excretion (2 hours)		—	—	—	—	—	65%
(kidney function)							
Fluid intake (water, glucose & saline — cc)		2000	2000	3000	4800	4600	3600
Transfusions (citrated whole blood — cc)		1000	1500	850*	—	—	—
Urinary output (cc)		670	700	1250	1270	1880	2170

* Plasma

The clinical and pathologic changes that occur in the "hepato-renal syndrome" have been collected and described by Boyce, and by Olin and Helwig. These changes are most likely to follow extensive crushing or gunshot injuries of the liver rather than stab or incised wounds. In some of these cases of severe trauma to the liver, hyperpyrexia and alterations in the blood chemistry follow the injury in a few hours. The rise in temperature is often very high and is associated with a rapid, weak pulse. Restlessness, collapse and delirium may accompany the high febrile reaction.

The alterations in the blood chemistry often appear early and usually consist of an increase in the nonprotein nitrogen and creatinine. Icterus may occur. The blood glucose, carbon dioxide combining power, cholesterol and plasma chloride levels have not been altered in the few cases in which they have been determined.

Alterations in renal function are likely to occur also and may appear early, as in our case, or be delayed. Oliguria, or anuria, and the appearance of red blood cells, white blood cells, casts and albumin in the urine are the usual findings.

In the case reported the elevation in hemoglobin and number of erythrocytes (120 per cent hemoglobin, 5.65 million red cells) on the day of the injury was probably the result of hemoconcentration that accompanies shock.

There was no evidence of such concentration during the period of collapse which occurred the day following operation when the extreme hyperpyrexia was present. The diminution in the level of plasma protein in the blood (4.55 Gm per 100 cc of blood) on the day following the injury most likely resulted from loss of plasma from the blood stream by reason of shock and hemorrhage. The plasma protein levels might well have been lower had not transfusions of blood and plasma been given.

The critical condition of patients with severe injury to the liver, and the urgent necessity for active therapy, have made it difficult or impossible, as in the case described above, to perform tests of liver function early in the course of the illness. The pronounced oliguria rendered the simple intravenous hippuric acid test impossible of performance, and the necessity for multiple venipunctures almost prohibits the use of the dye excretion or serum bilirubin tests while active therapy is in progress. Perhaps future cases of less severe trauma to the liver will permit more adequate examination for disturbances of liver function by serial Quick (hippuric acid) tests. The rose bengal excretion test made on the sixth day (Table I) on the case herewith reported, indicates remarkably good hepatic excretory function at that time, and the phenolsulfonphthalein test done on the same day shows evidence of good recovery of renal function. The prothrombin time of the blood was 80 per cent of normal on the third day following the injury and 100 per cent on the fifth day. These determinations were made relatively late, after numerous transfusions of blood had been given.

The pathologic changes in the livers of patients who have died of the traumatic "hepatorenal syndrome" are said to be degenerative, consisting of edema and necrosis, and to be confined principally to the cellular portions of the traumatized region. Diffuse, degenerative renal lesions have also been described and are usually greatest in the convoluted tubules.

Orr and Helwig attempted to explain the "hepatorenal syndrome" following trauma to the liver by suggesting the possibility that a soluble toxin is produced as a result of necrosis of the liver and that this toxin may produce injury to the kidney. They commented, however, that the "explanation of the causative factor or factors and the mechanism of their action upon the liver and kidneys must be determined by future investigation."

Apparently, Boyce also believes that a toxin is elaborated as a result of the degeneration of injured liver tissue (liver autolysis) but feels that the renal injury may be due to an "increase of its normal detoxifying duties, which are increased by failure of the detoxifying function of the liver, rather than by any specific action of the toxin."

Collier, in his discussion of Orr and Helwig's paper (1939), suggested that the azotemia and oliguria might be explained entirely on a basis of such alterations in physiologic processes as shock, dehydration, alkalosis, hypochloremia, hyponatremia, etc., rather than by the action of a specific toxin generated in the damaged liver. Other authors have suggested the possible

rôle of anaphylaxis and of infection, in attempting to explain this condition

The sequence of events and the findings in our case appear to justify its designation as an example of the so-called "hepato-renal syndrome" following hepatic trauma. The patient was a young healthy adult. He sustained an injury in which the trauma apparently involved the liver exclusively. This injury was accompanied by intra-abdominal hemorrhage and profound shock. After a favorable response to therapy for shock, celiotomy was performed under ether anesthesia. There was profuse bleeding from a long deep laceration in an inaccessible part of the right lobe of the liver, which was controlled by the temporary application of a hot moist pack. Following the operation the patient reacted well at first, although the temperature remained around 103° F. About 30 hours after the injury an unusual clinical picture developed characterized by hyperpyrexia (highest 107.8° F), rapid pulse of poor volume, hypotension (systolic pressure from 70 to 80), oliguria, retention of nitrogen, cold moist, cyanotic skin and delirium with great restlessness evidenced by wild thrashing movements. Therapy consisted of continuous inhalations of oxygen and infusions of whole blood, plasma, glucose and physiologic saline solutions. After a stormy convalescence of several days the patient recovered completely. There was no evidence of infection, and nothing to suggest anaphylactoid or transfusion reactions.

Speculation regarding the reaction that occurred in this case brings up the possibility that shock with hypoproteinemia, diminished blood volume with decreased circulatory efficiency and hypoxia in the body tissues, including those of the liver and kidneys, may well have played a contributory part in the syndrome that followed. The trauma of the exploratory operation, the application of the hot pack to the damaged liver, and the use of ether as an anesthetic agent must also be considered as possible contributory factors in this case. Hypochloremia was not present, nor did Ori and Helwig find it in their cases. We feel that dehydration probably did not play a part in this case, although the fluid intake during the first two 24-hour periods was not high (3000 and 3500 cc, respectively including the blood transfusions). Infection apparently played no part. At no time after operation were there signs of peritonitis, infection in the wound or infection in the bile which drained. Anaphylaxis and transfusion "reaction" were considered but thought to be very unlikely.

The possibility that some other factor (or factors) may be responsible for the production of this sudden, violent "hepato-renal syndrome" which sometimes follows severe trauma to the liver must also be considered. It may finally prove to be some series of physiologic and biochemical alterations, as suggested by the discussion of Collier. Or perhaps it is the soluble nephrospecific toxin originating in the liver, as suggested by Ori and Helwig, or a toxic product of autolysis of the liver as postulated by Boyce. At present the final explanation is not evident.

Whatever the chief cause of the "hepatorenal reaction may eventually prove to be, at the present time the prevention and treatment of this syndrome would appear to be best directed toward the correction of those aspects of the physiologic and biochemical alterations that are now known, even though they may prove to be only contributory factors. The active treatment of shock with transfusions of blood or plasma given repeatedly and in large amounts if necessary to replace lost blood restore the blood protein level and thereby maintain adequate blood volume and circulatory efficiency, is of primary importance. Transfusions also provide protein and prothrombin in readily available form if deficiencies develop. An atmosphere rich in oxygen should be provided in order to insure, if possible, adequate oxygenation of the tissues, including those of the liver and kidney. The intake of fluid must be carefully and correctly determined, enough but no great excess of crystalloid solutions is provided. Hypochloremia has not been a factor in these cases. The requirements for sodium chloride solutions are, therefore only for maintenance unless, for some other reason, vomiting for example deficiency should develop. "Glucose is the sheet-anchor of therapy in patients with hepatic and biliary tract disease" (Boyce). This probably holds true for acute trauma to the liver as well as other conditions affecting its function and glucose should therefore, be provided in reasonably large amounts. Every infusion of fluid (except the blood transfusions) given intravenously to the patient with this type of trauma should probably contain glucose. Physiologic saline is included in some of the infusions in amounts sufficient to provide for the calculated need for sodium chloride. Since there is some indication that dehydrocholic acid (Decholin) therapy may improve function of the liver when it is depressed (Boyce) and probably that this therapy causes improved function of the kidneys through improved hepatic function, it would appear reasonable to try it in these cases of severe injury to the liver. It was not used in the authors' case.

The operation to be performed in cases of severe trauma to the liver has been adequately discussed elsewhere. Many factors determine the decision as to whether or not to operate, the selection of the proper time for operation, and the procedure to be carried out. The importance of shock and hemorrhage, the type and probable extent of the injury to the liver, and the possibility of other internal injuries must be carefully considered in each case. Ordinarily we should treat shock and then operate as soon as a reasonably favorable response is obtained. Occasionally, however evidence of continuing internal hemorrhage may necessitate operation after therapy for shock has been followed by little or no improvement in the patient's condition. In this connection the use of transfusions of blood before, during and after operation may be of considerable assistance. Oxygen therapy is also employed, and the anesthetic agent should be selected and administered with the idea of adequate oxygenation in mind. It is probably superfluous to advise that the least possible trauma be inflicted upon the patient and especially the

already damaged liver, during the course of the operative manipulations. The question of whether to suture the liver, pack it, leave it alone, or possibly resect the damaged portion (as suggested by Tinker, and Boyce) must be decided in each case, depending on the condition of the patient and the location and extent of the injury. In some cases it may be possible and advisable to suture lacerations in the liver. Packing should be avoided, if possible, as it almost always leads to infection, or secondary bleeding, if it is left in place for any considerable length of time. In cases in which the necrosis is extreme, Boyce advocated resection of the traumatized hepatic tissue as an attempt to prevent "intoxication" from "liver autolysis." He mentioned the probable value of the thrombin spray of Warner as an effective means of hemostasis during resection of the liver. His thesis is interesting and the procedure of resection of traumatized liver may become a reasonable one, if the idea proves to be as true as it appears to be from his experimental and clinical observations. The critical state of the patient from shock and hemorrhage, and the extent and location of the injury to the liver are factors that must be considered, in addition to that of hemostasis in the liver, before resection of traumatized liver is undertaken. The duration of the operation is also a matter that may influence the outcome in a case of severe injury to the liver. Even though the surgeon is trained in the niceties of the Halsted method of surgical procedure in which gentleness, deliberation and thoroughness become habitual through many years of training, he may be inclined to agree with Boyce, who also cited Prey and Foster, that the operation in cases of severe trauma to the liver should proceed as expeditiously as is reasonably possible, mainly in order that the patient be spared the effects of prolonged anesthesia. Thoroughness, gentleness, and hemostasis, however, should not be sacrificed for the sake of shortening the operating time because shock may be precipitated or increased by rough handling and extra bleeding, and dangerous injuries to other viscera may go undiscovered in perfunctory exploration of the abdomen.

SUMMARY

A case of severe trauma to the liver accompanied by shock and hemorrhage is reported. After favorable response to therapy for shock and operation for control of hemorrhage the patient responded well for several hours. The following day about 30 hours after injury, he developed extreme hyperpyrexia, azotemia, oliguria, collapse with cold, moist, cyanotic skin, hypotension, rapid thready pulse and delirium. The main part of his treatment consisted of transfusions of blood and plasma, continuous inhalations of oxygen and parenteral glucose therapy. The patient recovered.

REFERENCES

- ¹ Boyce, F. F. The Role of the Liver in Surgery. Pp. 3-97, Charles C. Thomas, Springfield, Ill., and Baltimore, Md., 1941.
- ² Furtwaengler, A. Diffuse Rindenekrose Bieder Nieren nach Leberruptur. Krankheitsforschung 4, 349-374, June 1927.

- ³ Heyd, C G The Liver and Its Relation to Chronic Abdominal Infection ANNALS OF SURGERY, 79, 55-77, January, 1924
- Idem* Hepatitis in Relation to Inflammatory Disease of the Abdomen A Clinical and Laboratory Study Am Jour Obst and Gynec, 7, 413-430, April, 1924
- Idem* Hepatitis A Condition Associated with Gallbladder Disease S G & O, 39, 66-72, July, 1924
- Idem* "Liver Deaths" in Surgery of the Gallbladder J A M A, 97, 1847-1848, December 19, 1931
- ⁴ Orr, T G, and Helwig, F C Liver Trauma and the Hepatorenal Syndrome ANNALS OF SURGERY, 110, 682-692, October, 1939
- Idem* Is There a Hepatorenal Syndrome? Surgerv, 7, 136-137, 1940

PLATYBASIA WITH INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM

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PLATYBASIA (synonyms—basilar impression, basilar invagination) is a deformity of the occipital bone and the upper cervical vertebrae. The nature and degree of the deformity varies greatly but, essentially the foramen magnum is displaced upward into the cranial cavity and the upper cervical vertebrae are dislocated upward and forward into the cranial depression. In the majority of cases the deformity is due to a congenital defect in development of the occipital bone, atlas and axis, but in a smaller number the deformity is acquired as a result of some pathologic process that occurs in the bones of the region.

In platybasia the relative location, size and shape of the foramen magnum as well as that of the upper cervical canal is altered, and the posterior cranial fossa is diminished in capacity. In some this may not produce untoward symptoms at any time in life. In others, it may be associated either with congenital anomalies of the nervous system or be the direct cause of progressive nervous changes, sometimes both conditions exist. The resultant clinical manifestations may be confused, principally, with those occurring in conjunction with neoplasms of the posterior fossa or upper cervical canal, hydrocephalus, syringomyelia, syringobulbia, multiple sclerosis and spinocerebellar disease.

The four cases reported here will serve to demonstrate various etiologic factors, the structural changes and the nervous manifestations associated with platybasia. The results of operative decompression indicate the value of operation in alleviating symptoms and in staying the progress of the changes in the nervous system.†

Case 1—*Platybasia and congenital deformity of the upper three cervical vertebrae. Neurologic signs interpreted as multiple sclerosis appeared at age 31, and progressed to marked disability. Operative decompression of the cerebellum and upper cord was followed by considerable improvement and partial rehabilitation after two years.*

H. DeS., white male, age 37, was admitted to the New York Hospital, January 23, 1940, complaining of weakness of all extremities, progressing for six years, almost to complete incapacitation.

In 1934, he first noticed weakness and clumsiness in the right upper extremity. Prior to this time his history had been unremarkable. Later in the same year his gait became staggering and he had sensations "akin to numbness" in his right hand and toes.

† Only the first three cases were presented at the meeting of the New York Surgical Society.

He was first examined in this hospital in October, 1936, when he was found to have coarse horizontal nystagmus, loss of fine motions, and weakness in the right hand, impaired discriminatory sense in the right hand, sluggish abdominal reflexes, unsteady gait, inability to stand with feet together, unsustained ankle clonus bilaterally, and a positive toe-stretch and Chaddock sign bilaterally. Cerebrospinal fluid findings were normal. A tentative diagnosis of multiple sclerosis was made. The same diagnosis was made in two other clinics during the ensuing four years, and he became steadily worse under various forms of treatment.



FIG. 1.—Case 1. Photograph showing a male, age 37, with congenital platybasia.

FIG. 2.—Case 1. Lateral roentgenogram showing rudimentary development of the occipito-atlanto-axial region "occipitalization" of the atlas, upward dislocation of the odontoid process, and fusion of the second and third vertebrae.

In 1940, when readmitted to this hospital, the weakness and clumsiness in the extremities had progressed to the point where he was totally unable to dress himself, and even had great difficulty in feeding himself. He walked with a broad, staggering gait requiring the partial support of another person. Vision often became blurred particularly if he looked downward or sidewise. Vertigo occurred regularly on changes in position of the head. He also found that movement of the head caused a dull aching pain in the neck and back of the head.

Physical Examination—The patient was heavily built and tended to be obese. The neck was short and thick and the head appeared to be thrust forward (Fig. 1). Speech was slightly dysarthric. There was coarse nystagmus on moving the eyes in any direction. The tongue deviated to the left. Other functions of the head and neck were normal.

In the upper extremities there was weakness in the hand grips more pronounced on the right. Rapid rhythmic movements were badly performed. Point to point tests were grossly dysmetric. The deep reflexes were very active and there was a positive finger-stretch reflex bilaterally. Two-point discrimination, identification of objects by feel, and position sense were absent in both hands. Vibratory sense was diminished. Other forms of sensation were normal.

Sensation over the trunk was normal. The abdominal reflexes were sluggish and quickly exhausted.

In the lower extremities alternating movements and point-to-point tests were poorly performed. Gait was slow, staggering and broad based. Standing with feet together was impossible. The knee and ankle jerks on the left were exaggerated. Plantar responses were abnormal bilaterally. There was marked impairment of position and

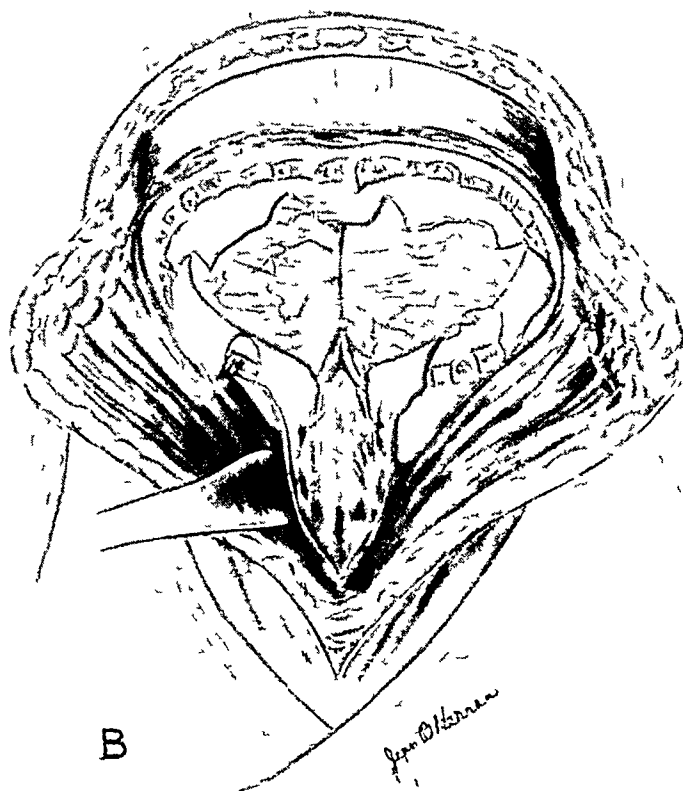
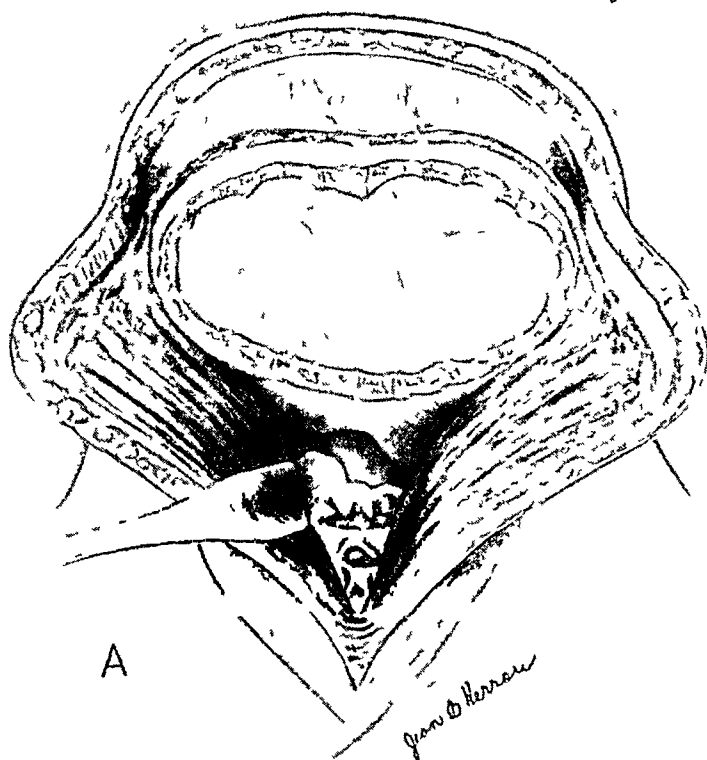


FIG. 3—Case 1. (A) View with dura over cerebellum partly exposed showing thickness of the occipital bone at the foramen magnum due to "occipitalization" of the atlas. The arch of the axis is asymmetrical and its lumen narrowed. (B) View after opening the dura showing flattening of the cerebellum, narrowing in region of the foramen magnum, atrophic appearance of the upper cord and transverse groove across cord at the level of the arch of the axis.

vibratory sense and moderate impairment of deep pain sense, other sensations were normal

Roentgenograms (Fig 2) showed absence of a discernible first cervical vertebra, due probably to its partial fusion with the occipital bone, thickening of the posterior margin of the foramen magnum, moderate protrusion of an abnormally long-appearing odontoid process into the foramen magnum, partial fusion of the laminae and bodies of the second and third cervical vertebrae

Operation—January 27, 1940 (Fig 3) Local procaine anesthesia was employed, and a suboccipital and upper cervical decompression was performed. The attachment of the occipital muscles was low on the skull and exposure of the occipital bone was difficult. The foramen magnum appeared unusually small, and the bone about it unusually heavy. A flange of bone existed on the right margin of the foramen magnum, the result of fusion of the lamina of the first vertebra. The arch formed by the laminae of the second cervical vertebra appeared to be unusually narrow and to constrict the dura. After removal of a fairly large segment of the occipital bone, the foramen magnum was opened widely and the first two (second and third) cervical arches were also removed. The dura, particularly at the level of the foramen magnum, was abnormally thick (2 to 3 mm) and tended to constrict the structures within it. After the dura was opened over the cerebellum an upper cord examination showed the flattened vermis and hemispheres of the cerebellum. The cisterna magna did not exist. The cerebellar tonsils were small and atrophic. The upper part of the exposed cord was void of its normal configuration and the pia arachnoid was adherent. At the level of the first intact vertebral arch there was a transverse groove in the dorsal surface of the cord that had a brownish pigmentation as though resulting from pressure of the neural arch. Below this point the cord appeared normal. The wound was closed but the dura was left open for decompression.

Postoperative Course—Recovery from operation was uneventful and three weeks after operation the patient was thought to be improved, in that there was less discomfort in the neck, the "feeling of heaviness" in the upper extremities was less, position sense in the upper extremities was improved, and there was greater steadiness in standing and walking.

Follow-Up—In the two years following operation improvement was gratifying. He was able to dress himself, walk about without assistance, and work with tools as a handy man. He was free of discomfort in the neck and of vertigo. Examination showed that none of the motor or sensory changes observed prior to operation had disappeared but all were improved.

COMMENT—The steady progression of the neurologic symptoms during the six years the patient was under observation was striking. The rôle of the craniovertebral compression of nervous structures as a cause of the symptoms and the value of decompression, are incontrovertible in view of the marked improvement that followed operation. There is no reason to doubt that the skeletal anomaly was congenital but just why symptoms did not appear before age 30 is not obvious.

Case 2—*Platybasia and congenital deformity of cervical spine. Neurologic signs simulating syringomyelia were slowly progressive for 16 years. Operative decompression of the cerebellum and upper cord was followed by improvement.*

G J, white, male, age 43, was admitted to the New York Hospital, July 7, 1941, complaining of impaired sensation and recurring infections in the fingers of the left hand.

During childhood he had severe rickets, as did several other children in his large family. Otherwise his health was not noteworthy until 1925 (at age 27), when he developed painless infections in two fingers of the left hand and the last phalanx of each was amputated. The ends of two other fingers of this hand were lost under similar

circumstances during later years. Because of an infection in the left thumb he was first examined in this hospital in 1939, when he was found to have deformity and muscular atrophy of the neck, possibly slight wasting in the muscles of the left hand, absent tendon reflexes in the upper extremities, and impaired pain and temperature sense in the neck and upper extremities, more pronounced on the left. *Clinical Diagnosis* Syringomyelia.

When admitted to the hospital in 1941 he added to his previous complaints those of more recent periods of vertigo, drooping of the left shoulder, increase in his neck-size and unsteadiness when working on scaffoldings.

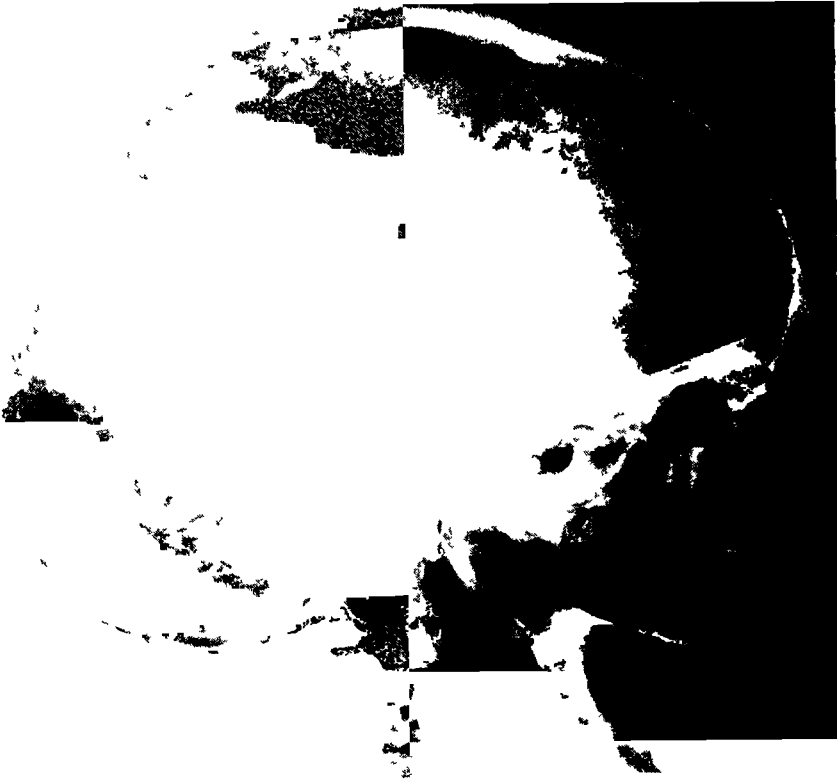


FIG. 4.—Case 2. Lateral roentgenogram showing long, narrow shape of the cranial cavity, prominence of the petrous ridges, upward displacement of the clivus Blumenbachii, inclusion of the arch of the atlas in the foramen magnum, and upward displacement of the odontoid process.

Physical Examination—The patient was of short, muscular build. The neck was short, thick and asymmetrical. The head was large in its biparietal measurement, and was held with the chin tilted to the left. There was slight limitation of motion in turning and extending the head on the neck. The left shoulder drooped, the angle between it and the neck was obliterated and the left sternocleidomastoid muscle was weak. There was a long S-shaped scoliosis involving the cervicodorsal spine. There was slight wasting as well as fibrillations of muscles in the neck and shoulder girdle on the left.

There was coarse nystagmus on lateral movement of the eyes, more pronounced on looking to the left. The protruded tongue deviated to the left and speech was slightly dysarthric. There was impairment of pain and temperature sense over the posterior part of the head, neck and shoulder on the left. Other functions of the head and neck were normal.

In the upper extremities the only demonstrable palsy was slight wasting of the muscles of the ulnar side of the left hand. The tendon reflexes were absent bilaterally. There was partial to total loss of pain and temperature sense in the left extremity and slight impairment of these sensations in the right. Other forms of sensation were pre-

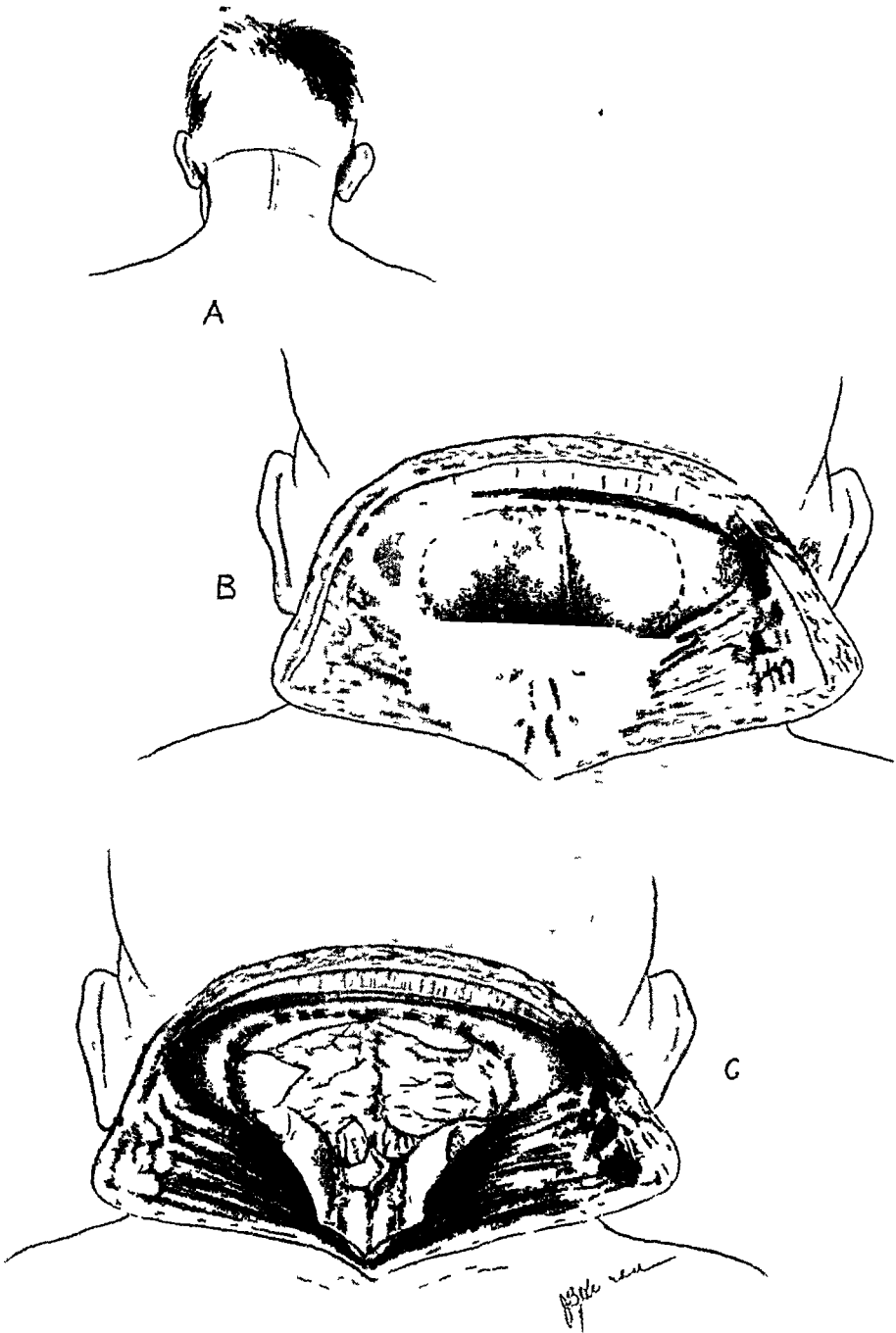


FIG 5—Case — (A) Type of operative incision. (B) View with occipital bone and upper three cervical vertebrae exposed showing asymmetry and concavity of occipital bone, and partial inclusion of the arch of the atlas in the foramen magnum. (C) View after opening the dura showing compressed appearance of the cerebellum, herniation of the cerebellar tonsils, narrowing of the foramen magnum, an aberrant artery and bulging at the junction of the medulla and cord.

served. The distal phalanges of all but the thumb on the left were absent while the thumb was swollen, deformed and ulcerated.

Sensation over the trunk was normal and the abdominal reflexes were absent. In the lower extremities the findings were normal but for a positive Romberg sign and impairment of position sense in the feet.

The cerebrospinal fluid pressure, manometric studies and laboratory tests were normal.

Roentgenograms (Fig. 4) showed partial fusion of the bodies of the fifth and sixth cervical vertebrae, protrusion of the odontoid process into the foramen magnum, partial inclusion of the neural arch of the atlas inside the foramen magnum, unequal prominence of the petrous ridges, and upward displacement of the clivus blumenbachii.

Operation—August 8, 1941 (Fig. 5). Under ether anesthesia, a suboccipital and upper cervical decompression was performed. The skull between theinion and the foramen magnum was flattened and slightly concave. The middle ridge of bone was displaced to the right indicating an asymmetry of the posterior fossa. The neural arch of the atlas was almost hidden inside the foramen magnum. A segment of the occipital bone was removed and the foramen magnum opened widely. The arches of the first three cervical vertebrae were also removed. The dura, which at the foramen magnum was found to be three to four millimeters thick, was opened to expose the cerebellum and upper cord. The cerebellar hemispheres had a flattened and atrophic appearance. Near the foramen magnum there was no space for the cisterna magna, as the dura was tightly apposed to the cerebellum and to small tips of flattened cerebellar tonsils that had herniated through the foramen and fitted snugly against the cord. The uppermost portion of the cord bulged slightly in its posterior aspect, and an aberrant artery curved over it to the right. This part of the cord probably represented an heterotopia, for neither it nor the normal appearing cord below it as far down as the fourth segment felt cystic or yielded fluid on aspiration with a fine needle. The course of the first three pairs of cervical nerve roots was normal but the spinal accessory nerves, particularly the left, were subjected to considerable pressure in the constricted region of the foramen magnum. There were no extensive arachnoid adhesions and it did not appear that the spinal fluid pathways were thus obstructed. The wound was closed but the dura was left open for decompression.

Postoperative Course and Follow-Up—Recovery from operation was uneventful and the patient resumed work as a carpenter one month later. Three months after operation he volunteered that he felt steadier on his feet and less clumsy in his upper extremities than he had for several years. No special improvement could be demonstrated on examination.

COMMENT—The etiology of the platybasia in this case, in view of the coexistence of fused cervical vertebrae, was probably a congenital defect in development of the occipital bone. Rickets has been mentioned by others as a theoretic etiologic factor in platybasia, but its rôle in this case is doubtful.

The majority of the neurologic findings might be attributed to syringomyelia or syringobulbia, and sometimes these congenital conditions have been found to be associated with development defects of the craniovertebral skeleton. However, no syrinx could be discovered at operation and it is likely that at least some of the neurologic changes were the direct result of the cranial deformity.

Case 3—*Platybasia developing between the fourth and twelfth years in a child with osteogenesis imperfecta. Neurologic signs appeared insidiously after age ten. Operative decompressions of the cerebellum and upper cord was followed by improvement.*

A. M., white, female, age 12, was admitted to the New York Hospital, June 9, 1941 because of cellulitis of the leg.

The girl had first been examined in this hospital for fractured tibia when she was four years old. She had had a spontaneous fracture of the humerus in the first month of life, and had had a succession of at least 20 additional fractures during the succeeding four years. A diagnosis of osteogenesis imperfecta was made and various forms of treatment were employed while she was being followed periodically in the Out-Patient Department. The frequency of fractures diminished and none had occurred after age eight.

At the time of admission to the hospital in 1941, it was brought out in the history that for a year or more speech had had an indistinct and monotonous quality. Also, there was occasional choking and difficulty in swallowing liquids.

Physical Examination—She was of average size and development for her age. However, the neck was rather short and broad and the head was held with the chin tilted to the left. The head was unusually broad in its biparietal measurement. The sclerae were blue. There was nystagmus on lateral gaze and weak convergence of the eyes. The tongue was protruded to the left, and on the left side was markedly atrophic; there were also fibrillations and atrophy on the right side of the tongue. In addition to thickness, the speech had a nasal quality and the palate moved poorly. Other functions of the head and neck were normal.

There were numerous deformities of the extremities, results of former fractures, but most of these were insignificant. Motility functions were fairly good except for moderate incoordination in point-to-point and rapid rhythmic movements in the upper extremities. Station and gait were not remarkable. The deep reflexes on the right were more active than on the left, and the right plantar response was abnormal. Sensation was everywhere normal but for reduction in position sense in both great toes.

Roentgenograms taken at various times of life had shown the decreased calcium content of all bones—characteristic of osteogenesis imperfecta. The configuration of the skull and cervical spine was normal in 1933 (Fig 7). The skull plates, taken in 1941 (Figs 7 and 8), however, showed the vault to be widened and flattened and the floor of the skull behind the sella turcica was invaginated, especially above the atlanto-occipital articulations. The cervical vertebrae were not deformed but the atlas was partly hidden in the invagination of the base of the skull and the odontoid process protruded into the foramen magnum.

Operation—June 26, 1941 (Fig 9). Under ether anesthesia, a suboccipital and upper cervical decompression was performed. The skull between theinion and foramen magnum was flat, even slightly concave, and it formed an acute angle with the line of the spinal column, which made the foramen magnum seem unusually deep. The arch of the atlas lay almost completely within the foramen magnum and could be seen clearly only after removal of a segment of the occipital bone and opening of the foramen magnum. Even after removal of the laminae of the atlas and axis the dura at the level of the foramen magnum dipped acutely, as if from long indentation by the arch of the atlas, and certainly appeared to be constricting the structures within. The dura in this region was about two millimeters thick. When the dura had been incised to expose the cerebellum and upper cord, examination showed the cerebellar hemispheres to be generally small and atrophic looking, with very little of the vermis showing and almost complete obliteration of the cisterna magna. The tonsils of the cerebellum were greatly elongated and extended down the spinal cord to the level of the second cervical arch. The left tonsil overlapped the right, suggesting that there was more distortion of the base of the skull on the left side, a supposition which would be compatible with the greater twelfth cranial nerve palsy on the left and right-sided corticospinal tract signs.

There were no adhesions in the region, the cord had a normal appearance, and the course of the cervical nerve roots was normal. The wound was closed, but the dura was left open for decompression.

The bone removed at operation was not remarkable from a gross standpoint, but microscopic examination showed the faulty development characteristic of osteogenesis imperfecta.

FIG 6



FIG 7

FIG 6—Case 3. Lateral roentgenogram taken at age four (1933) showing poor calcification characteristic of osteogenesis imperfecta but normal configuration in the basilar region.

FIG 7—Case 3. Lateral roentgenogram taken at age 12 (1941) showing the acquired platybasia (compare with Figure 6). Note the long narrow shape of the cranial cavity, the prominence of the petrous ridges, the elevation of the clivus, the displacement of the atlas and axis into the basilar depression, and the upward displacement of the atlas and axis into the basilar depression.

Postoperative Course and Follow-Up—Recovery from operation was uneventful. Examination after five months showed a soft, flat area of decompression. There was no appreciable change in speech or in configuration of the tongue. The involvement of the corticospinal tract on the right and the impaired position sense in the toes could no longer be detected.



FIG 8—Case 3. Anteroposterior roentgenogram taken at age 12 (1941) showing a wide biparietal distance, bulging of the floor of the posterior fossa above the occipitoatlantal articulations, displacement of the odontoid process to the left of the midline and the abnormal appearance of the petrous ridges.

COMMENT—There is conclusive evidence here that the flattening of the base of the skull was not due to a congenital malformation of the occipital bone. The evidence indicates that the soft, poorly calcified skull had become indented at its base, probably from sheer weight of the growing head upon the spine. The appearance of the skull is indeed comparable to what might occur if weight were put upon the top of a flexible skull causing it to elongate, broaden, and indent at its base. The resulting distortion of the brain stem, diminution in the capacity of the posterior fossa and narrowing of the foramen magnum would amply account for any changes in the nervous system. Because it was assumed that injury to the nervous system would increase,

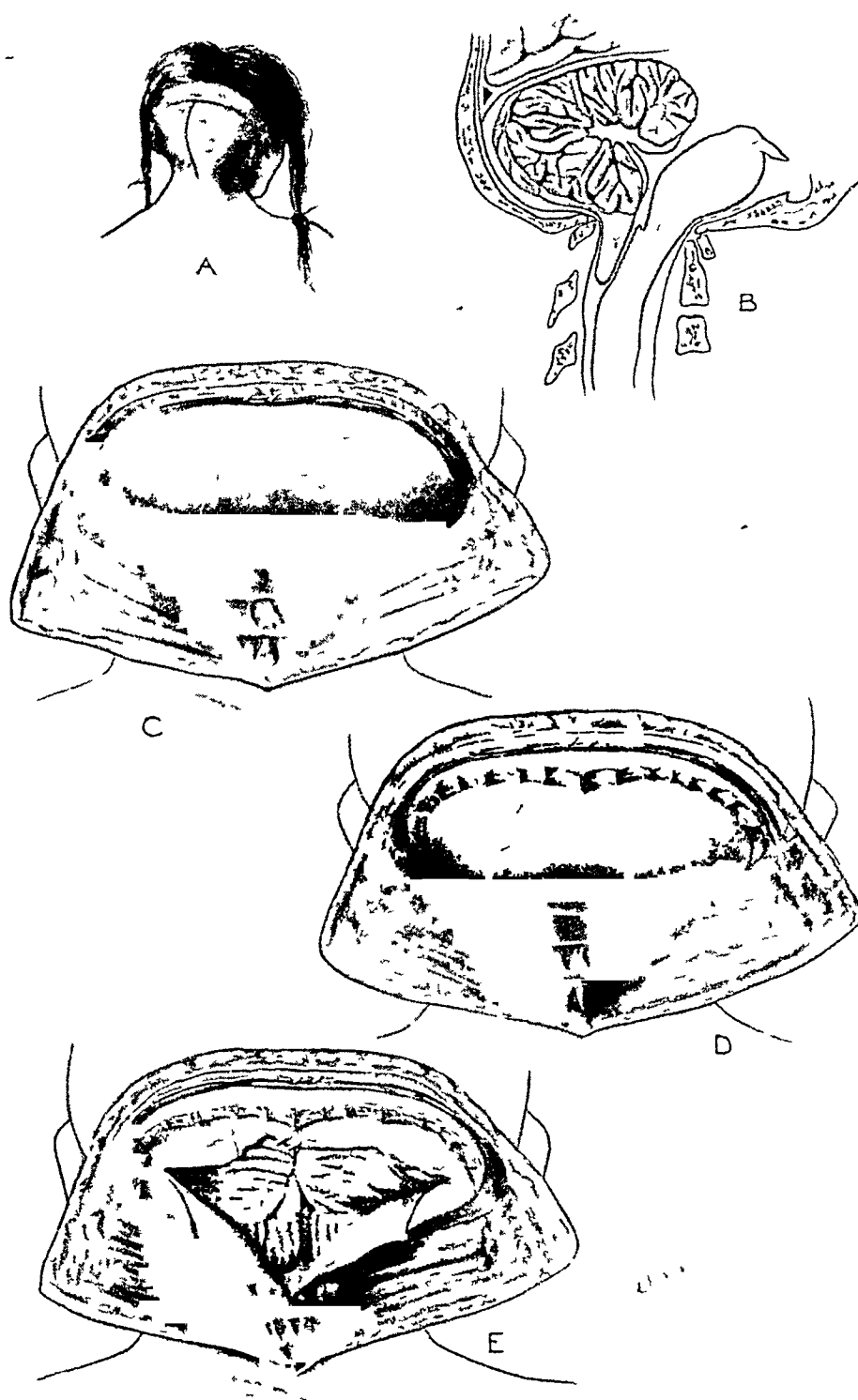


FIG. 9—Case 3. (A) Type of operative incision. (B) Diagrammatic representation of the nature and effects of the craniovertebral abnormality. (C) View with occipital bone and upper three cervical vertebrae exposed showing concavity of the occipital bone and partial inclusion of the arch of the atlas in the foramen magnum. (D) View after resection of the occipital bone and opening of the foramen magnum showing the arch of the atlas maintaining the constriction of the dura at the foraminal opening. (E) View after resecting the first two neural arches and opening the dura showing the flattened cerebellum, absence of the cisterna magna, and unequal herniation of the cerebellar tonsils into the cervical canal.

decompression was employed even though the existing signs were not advanced. The disappearance of the signs of diseased pyramidal tract on the right side of the body and the return of position sense in the toes are evidences of improvement.

Case 4—*Platybasia developing in a middle-aged woman with Paget's disease of the skull. Neurologic signs appeared insidiously and advanced steadily over a period of two years. Operative decompression of cerebellum and cord.*

H. C., white, female, age 47, was admitted to the New York Hospital, January 5, 1942, because of headache, vertigo and increasing difficulty in walking. She had been observed periodically in the Out-Patient Department for several months, but entered the hospital when symptoms became severe.

She had been in good health prior to the beginning of enlargement of her head in 1933 (at age 39). A diagnosis of osteitis deformans (Paget's disease) of the skull was made by her physician, and for eight years the head had steadily enlarged. No untoward symptoms appeared until the last two years of this period.

Pain in the back of the head and neck, which was the first symptom, was, in the beginning, mild and unimportant but, later, it became severe. It was induced by coughing, straining, and laughing. It was acute and spread up fan-wise from the back of the neck over the back of the head to the vertex, lasting five to ten minutes.

Gait, which at first was but slightly unsteady, gradually became staggering, and motions in the upper extremities became clumsy. The right arm became weak, and the right foot had dragged during the past year.

The most recent and distressing symptom was paroxysmal vertigo which was induced by sudden turning of the head. The fear of inducing an attack led to holding her head in a fixed position.

Physical Examination—The patient was a slender, fragile looking woman, with a large asymmetrical head and a short wide neck. The neck was held stiffly and the head was moved cautiously. The eyes were slightly prominent and coarse nystagmus developed on lateral gaze which was greater on looking to the right. Hearing was diminished 25 per cent on the left and 15 per cent on the right. The muscles of the tongue showed a moderate degree of atrophy and fibrillations, and when protruded it deviated to the left. Speech was slightly thick and had a nasal quality. The right shoulder drooped. There was clumsiness in rapid rhythmic movements and in point-to-point tests of all extremities. Gait was slow, staggering and broad based. Romberg's sign was positive. There was an hemiparesis of moderate degree involving the right upper and lower extremities. Position sense and two-point discrimination was impaired in the right hand. There was a right hemihypalgesia, not including the face. Position sense was markedly impaired in both feet.

Significant laboratory studies showed normal serum calcium and serum phosphorus but a serum phosphatase of 25 to 30 units (normal is four units). Bleeding and clotting times were normal, but the plasma prothrombin was 18 per cent. The prothrombin value rose to 30 per cent and 70 per cent on successive days on administration of vitamin K (2-methyl-1, 4-naphthaquinone).

Roentgenograms of the skull, taken in 1934 (Fig. 10), showed characteristic changes of osteitis deformans and the early changes of platybasia. Roentgenograms of the skull taken in 1941 (Fig. 11), showed the results of marked indentation of the basi-occipital region and comparison with the earlier films disclosed the progression of this state. There was invagination of the posterior rim of the foramen magnum, narrowing of the posterior cranial fossa, upward and anterior displacement of the atlas and axis. Many other bones in the body showed increase in the trabecular pattern, scattered areas of density and cystic changes but the skull was most prominently involved by the disease and there was no collapse of vertebrae to account for any of the neurologic signs.

PLATYBASIA

FIG 10



FIG 11

FIG 10—Case 4 Lateral roentgenogram (retouched) taken at age 40 (1934) showing typical osteitis deformans and beginning platybasia which was asymptomatic (Courtesy of Dr. William Snow.)

FIG 11—Case 4 Lateral roentgenogram (retouched) taken at age 47 (1941) showing marked degree of platybasia. By comparison with Figure 10, note the greater narrowing of the posterior fossa and the increased upward displacement of the atlas and axis into the transverse foramina of the occipital bone.

Operation—January 8, 1942 (Fig 12) Under ether anesthesia, suboccipital and upper cervical decompression was performed. The operation was attended by an unusual amount of bleeding from the soft tissues and the bone, which required assiduous atten-

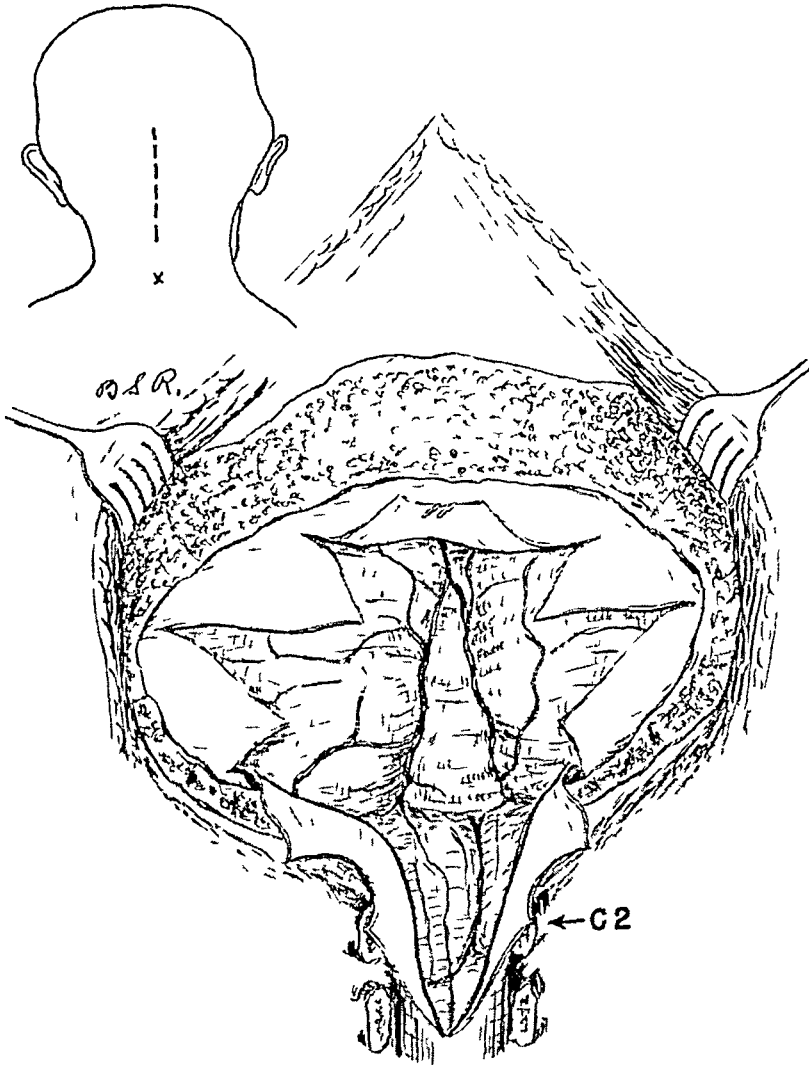


FIG 12—Case 4 Operative sketch showing the cerebellum and upper cervical canal exposed. Note the flattening of the cerebellar hemispheres, the wide vermis, grooved by the narrow foramen magnum, the absence of the cisterna magna, and the marked and unequal herniation of the cerebellar tonsils into the cervical canal. The inset shows the type of operative incision.

tion to hemostasis. The skull was from two to four centimeters thick, and so soft that the tip of a forceps could be plunged through it. The bone of the vertebral spines and arches was only slightly softer than normal. The arch of the atlas lay almost completely within the foramen magnum and appeared to be indenting the posterior rim of the foramen. The neural arches of the second and third cervical vertebrae were removed.

A fair-sized window in the occipital bone was rongeuired and curetted away. After the foramen magnum had been widely opened it was then possible to remove the arch of the atlas. In this region the dura was slightly thickened and gave the appearance of constricting the structures lying within it.

When the dura had been incised to expose the cerebellum and cord it was seen that the cerebellar hemispheres were flattened, the vermis was unusually wide and the cerebellar tonsils were herniated into the spinal canal to the upper level of the third cervical vertebra. The left tonsil was longer, more prominent and overlapped the right, suggesting greater distortion of the base of the skull on the left, a supposition which would be compatible with the right hemiparesis. There was no cisterna magna but after the dura had been opened an exchange of subarachnoid fluid between the cranial and spinal cavities could be demonstrated. There were no adhesions in the region, and what could be seen of the cord appeared normal. The wound was closed but the dura was left open for decompression.

Microscopic examination of the bone removed at operation showed the changes typical of osteitis deformans.

Postoperative Course—Recovery from operation was complicated only by edema of the neck during the first three days. Early indications pointed to improvement in all symptoms but the postoperative period is too short to evaluate results.

COMMENT—As in Case 3, this is unquestionably an example of acquired platybasia. The extreme softness of the skull and the increase in the weight of the head are conditions well suited to the development of platybasia. It is likely that this basilar deformity occurs in some degree in the majority of people with advanced osteitis deformans of the skull. The extreme narrowing of the posterior cranial fossa and of the foramen magnum, which can be seen on roentgenogram, and which was, in this case demonstrated at operation, possesses many possibilities for the production of neurologic symptoms. Whereas in the past the headache and various cranial nerve palsies frequently found to be associated with osteitis deformans have been largely interpreted as symptoms to be expected from such great thickening of the skull, it may develop that often such symptoms are the direct or indirect result of platybasia.

Decompression operation in patients with osteitis deformans is perhaps more hazardous than in others because these patients, in general, do not stand operations well, and there is the added difficulty in dealing with the increased vascularity of the bone and adjacent soft tissues. But this should be no contraindication to the operation if the signs and symptoms present warrant it.

DISCUSSION

Comparatively few references to platybasia have appeared in the Anglo-American literature^{1, 2, 3} and the deformity, though mentioned in European literature as far back as 1844,⁴ has never received the wide attention it deserves. Boogard,⁵ in 1865, Vuchow,⁶ in 1876, and Grawitz,⁷ in 1880, described in detail the changes in the skull. Homén,⁸ in 1901, correlated neurologic observations with postmortem study of the effects of pressure of the craniovertebral deformity upon nervous structures. Schüller,⁹ in 1911, by roentgenologic examination of the skull, first demonstrated basilar impression in

the living and, with an appreciation of the effects of the deformity upon the nervous system, described clinical examples having manifestations of medullary compression, cerebellar compression and cranial nerve involvement. Additional clinicopathologic studies have been reported by Sinz,¹⁰ Kecht,¹¹ Kiause,¹² Merio and Risak,¹³ Juhlin-Dannfelt,¹⁴ Ebenius,¹⁵ and in this country by Chamberlain,¹ Gustafson and Oldberg,² and List.³

The etiology of the craniovertebral deformity has from the time of its early description been ascribed largely to congenital maldevelopment or hypoplasia. List has described in detail a variety of anomalies of the occipital bone, atlas and axis in terms of the embryonic development of these structures. Case 1 in which there was synostosis of the atlas and occiput, is an example of congenital maldevelopment. Possibly Case 2 is also an example of prenatal maldevelopment, particularly in view of the synostosis of two of the cervical vertebrae but without this, one would give more consideration to the possible rôle of rickets in the patient's early life.

Most authors have suspected, with meager proof, that platybasia may be acquired as a result of such diseases as osteomalacia, rickets, syphilis, osteitis deformans and chronic increased intracranial pressure. Cases 3 and 4 are the only examples that have come to my attention in which the development of platybasia with accompanying neurologic symptoms has been demonstrated in the course of such disease. In each of these cases (one of osteogenesis imperfecta, and the other of osteitis deformans) the comparison of roentgenograms of the skull, taken years apart shows this development. In one instance the patient was a growing child, in the other a mature woman. A condition comparable in its effects may occur following fracture or dislocation at the occipito-atlanto-axial region; such a case has been reported from this clinic.¹⁶

Much depends upon roentgenologic examination in the diagnosis, for although there are many characteristic clinical features of the condition the final diagnosis in any case rests on the demonstration of the craniovertebral deformity by roentgenograms. Schuller¹⁷ has ably enumerated the characteristic changes that may be seen roentgenographically and most of the recent contributors have added to this aspect of the subject.^{15, 1, 2} The roentgenograms reproduced herewith emphasize most of the essential abnormalities.

The various roentgenographic changes seen in platybasia may be summarized as follows. In the lateral view may be seen: Rudimentary development of the occipito-atlanto-axial region, dislocation of the atlas and axis upward and forward, projection of the odontoid process above a line drawn from the posterior rim of the foramen magnum to the hard palate, upward displacement of the clivus blumenbachii, invagination of the posterior rim of the foramen magnum, high prominent position and more or less circular shadow of the petrous portions of the temporal bones and, a relatively long vertically narrow appearance of the cranial cavity.

In the sagittal views taken in the anteroposterior direction and in the "occipital projection" may be seen Asymmetry of the posterior cranial fossa and of the foramen magnum, upward dislocation of the atlas and axis, abnormal relation of the positions of the atlas and odontoid process to the lumen of the foramen magnum, abnormality of the atlanto-occipital articulations, prominence, unusual shape and asymmetry of the petrous portions of the temporal bones, and broad biparietal measurement of the skull

All patients with platybasia possess more or less the same appearance above the shoulders (Fig 1) The neck is distinctly short and thick, the hair line at the back is low The position of the head in profile is somewhat forward of the perpendicular axis of the body and in front view is usually tilted or turned This appearance is due largely to the craniovertebral deformity and need not be accompanied by limitation of movements of the head, pain or neurologic changes

Only when neurologic symptoms occur, does platybasia become anything more than a developmental curiosity It has been emphasized by other contributors to this subject that in congenital platybasia it is but reasonable to expect the presence of other congenital abnormalities^{3, 18} Thus, the occurrence of symptoms of syringomyelia in conjunction with platybasia may be only the result of a congenital "dysraphic" state which implicates both the nervous and skeletal systems, developmental disturbances in numerous mid-line structures have been found to accompany syringomyelia¹⁹ To accept this as the only explanation for the coexistence of platybasia and syringomyelic symptoms is failure to recognize the direct etiologic relationship that may exist between the skeletal deformity and numerous associated changes in the nervous system In the case of sensory dissociation of syringomyelic nature, for example, the changes may be the result of bony compression of the ventrolateral tracts of the medulla As a result of experience with a patient—in whom no syringomyelia was found at operation, and improvement followed operative decompression, Chamberlain stressed particularly "the tendency for basilar impression to masquerade as syringomyelia", Case 2 is comparable to this On the other hand, it is justly argued by Gustafson and Oldberg that when in the presence of platybasia, there exists an hydromyelic state of the central canal, the two conditions probably exist as cause and effect

Thus, in platybasia acquired changes in the nervous system may occur singly or in combination as a result of (1) direct pressure upon the brain stem, cranial nerves, cerebellum and cervical cord (2) embarrassment of the blood supply of these structures by adhesions or compression, or (3) interference with cerebrospinal fluid pathways

The flattened appearance of the cerebellar hemispheres, the absence of the cisterna magna, the protrusion of the cerebellar tonsils into the spinal canal, plus the dual constriction at the region of the foramen magnum demonstrated at operation, indicate the degree of general compression exerted upon these

nervous structures by the narrowed confines of the posterior fossa. Hydrocephalus of varying degree might be expected to accompany this state of affairs, and has been demonstrated by some observers^{2, 14}

The deformity of the nervous system found to accompany platybasia has been likened to the Arnold-Chiari deformity^{2, 7}. The latter is not a well defined malformation but is generally regarded as a downward elongation of the cerebellum and brain stem into the cervical portion of the spinal canal associated with spina bifida and myelomeningocele, hydrocephalus is frequently present as a result of obstruction of the fourth ventricle^{20, 21}. While the appearance of the brain and cord may in some respects be similar in the two conditions the mechanism producing the one is the antithesis of that producing the other. In platybasia the structures may be thought of as being pushed through the foramen magnum, whereas in the Arnold-Chiari malformation, they are pulled. The simple proof of the difference exists in the relatively normal course of the cervical nerve roots in the former and the abnormal upward course of the roots to their foramina in the latter.

This brief allusion to some aspects of the effects of platybasia serves to emphasize that any number of neurologic symptoms may result, depending upon the particular parts of the central nervous system that are impinged upon or otherwise disturbed by the craniocervical deformity. When the diagnosis has been established, operative decompression should be given thoughtful consideration. In the past, it has been assumed that platybasia and its associated neurologic symptoms were solely a medical curiosity, to be recognized in order that needless operation could be avoided^{14, 17}. Obviously, no operative procedure can rectify the invagination of the base of the skull or the displacement of the atlas and axis, but the removal of part of the squama of the occipital bone, the opening of the foramen magnum and the removal of one or two neural arches serves to enlarge the narrowed space occupied by the brain stem, cerebellum and upper cervical cord. Neither can it be expected that operative decompression will result in alleviation of all neurologic changes but the evidence indicates that improvement of existing symptoms and prevention of progressive changes may be hoped for.

Besides the four cases reported herewith, 12 others, having deliberate decompressive operations, have been reported^{1, 2, 3}. From an analysis of these cases two principles stand out: (1) That the dura must be opened to obtain satisfactory decompression and (2) that the less intradural manipulation of nervous structures the better. Personal experience has led to the belief that simple operative decompression is not hazardous and has much to recommend it when contrasted with the unfavorable prognosis of advanced compression of the brain and cord.

CONCLUSIONS

Platybasia is a craniocervical anomaly congenital or acquired that may be accompanied by changes in the central nervous system that result either directly from pressure or indirectly from the effects of the bony deformity.

Platybasia causes a characteristic appearance of the head and neck, and the neurologic symptoms masquerade as neoplasm of the posterior fossa or upper cervical canal, hydrocephalus, syringomyelia, syringobulbia, multiple sclerosis or spinocerebellar disease. The final diagnosis rests upon the roentgenographic demonstration of invagination of the basioccipital region of the skull and the upward displacement of the upper cervical vertebrae into this depression, producing narrowing of the posterior cranial fossa, foramen magnum and upper cervical canal. When neurologic symptoms are disabling or progressive operative decompression of the cerebellum and upper cord is beneficial in improving or staying the progress of the nervous changes. Simple operative decompression is not unduly hazardous.

REFERENCES

- ¹ Chamberlain, W. Edward. Basilar Impression (Platybasia). *Yale J Biol and Med*, 11, No. 5, 487-496, May, 1939.
- ² Gustafson, W. A., and Oldberg, E. Neurological Significance of Platybasia. *Arch Neurol and Psychiat*, 44, 1184-1198, December, 1940.
- ³ List, C. F. Neurologic Syndromes Accompanying Developmental Anomalies of Occipital Bone, Atlas and Axis. *Arch Neurol and Psychiat*, 45, 577-616, April, 1941.
- ⁴ Rokitsansky, C., cited by Ebenius, B.¹⁵
- ⁵ Boogard, J. A. Basilar Impression. Its Causes and Consequences. *Nederl tijdschr v geneesk*, 2, 81-108, 1865.
- ⁶ Virchow, R. Beiträge zur physischen Anthropologie der Deutschen, mit besonderer Berücksichtigung der Friesen. Berlin, G. Vogt, 1876.
- ⁷ Grawitz, P. Beitrag zur Lehre von der basilaren Impression des Schädels. *Virchows Arch f path Anat*, 80, 449-474, 1880.
- ⁸ Homen, E. A. Zur Kenntnis der rachitischen (?) Deformationen der Schadelbasis und der basalen Schadelhyperostosen. *Deutsche Ztschr f Nervenhe*, 20, 3, 1901.
- ⁹ Schuller, A. Zur Roentgen-Diagnose der basalen Impression des Schädels. *Wien med Wchnschr*, 61, 2594, 1911.
- ¹⁰ Sinz, P. Unterentwicklung des Hinterhaupt- und Keilbeinkörpers mit gleichzeitiger knöcherner Verbindung zwischen Atlas und Schadel als Todesursache. *Virchows Arch f path Anat*, 287, 641-650, 1933.
- ¹¹ Kecht, B. Zur Kenntnis der Klinik eines Falles von basilarer Impression. *Ztschr f d ges Neurol u Psychiat*, 141, 132-140, 1932.
- ¹² Krause, F. Chirurgie des Gehirns und Rückenmarks. Berlin, Urban & Schwarzenberg, 1911, vol. 2, 556-558.
- ¹³ Merio, P., and Risak, E. Klippel-Feilsches Syndrom, basilare Impression und endokrine Erkrankungen. *Ztschr f klin Med*, 126, 455-468, 1934.
- ¹⁴ Juhlin-Dannfelt, C. Platybasia. *Svenska lak-tidning*, 30, 470-473, May 5, 1933.
- ¹⁵ Ebenius, B. The Roentgen Appearance in Four Cases of Basilar Impression. *Acta radiol*, 15, 652-656, 1934.
- ¹⁶ Wade, Leo J. Pseudo-Platybasia. Rupture of the Transverse Ligament of the Axis with Displacement of the Odontoid Process and Compression of the Cervical Cord. *J Bone and Joint Surg*, 23, No. 1, 37-43, January, 1941.
- ¹⁷ Schuller, A. The Diagnosis of "Basilar Impression". *Radiology*, 34, 214-216, February, 1940.
- ¹⁸ Putnam, T. J. Discussion of Gustafson and Oldberg.²
- ¹⁹ Bremer, F. W. Die pathologisch-anatomische Begründung des Status dysraphicus. *Deutsche Ztschr f Nervenhe*, 99, 104-123, 1927.

- ²⁰ Penfield, W, and Coburn, D F Arnold-Chiari Malformation and Its Operative Treatment Arch Neurol and Psychiat, 40, 328-336, August, 1938
- ²¹ D'Errico, A Surgical Procedure for Hydrocephalus Associated with Spina Bifida Surgery, 4, 856-866, December, 1938

DISCUSSION DR IRA COHEN (New York) said that the cases presented by Doctor Ray represented almost a medical curiosity, inasmuch as platybasia is very rare, though not so rare as would be assumed from the paucity of cases reported in the literature. Cases are missed, first, because roentgenograms, if taken, are not carefully examined, and, secondly, for the more important reason, that in cases diagnosed as syringomyelia, intrinsic disease of the cord, or multiple sclerosis, roentgenograms of the upper cervical spine and skull are not taken and studied. The term "platybasia" was brought to the forefront after an article by Chamberlain a few years ago. Very probably "basilar invagination" is a more descriptive term. The platybasia itself is partially responsible for symptoms, but the majority of the symptoms are due to the deformity about the foramen magnum in which the skull and vertebrae combine. The symptoms are caused by compression, that is, narrowing of the foramen magnum, the pressure of the odontoid process, and very often there is thickening of the dura and bands of dura in this region plus herniation of the cerebellum into the spinal canal.

Doctor Cohen felt that Doctor Ray's third case was of particular interest because of the fact that the bony deformity was seen to develop while the patient was under observation, also, the onset of neurologic signs was seen to occur. There is no really adequate explanation for the development of symptoms in the second, third, fourth, or even fifth decade, from a condition which is congenital. If the bony deformity is static then, perhaps one must assume, with Chamberlain, that the young nervous system is more able to withstand the resulting pressure than is that of the adult. Otherwise, there is no real explanation of why symptoms develop late in life in some individuals. In this young girl, actual positive proof is offered that, under observation, there can be a change in the contour about the foramen with the onset of symptoms. Rickets, osteomalacia and many other conditions have been mentioned as a consequence. Doctor Cohen said he knew of no other case where such proof had been demonstrated.

The very appearance of the patients as they walked into the room was almost diagnostic.

EXTRALARYNGEAL DIVISION OF THE RECURRENT LARYNGEAL NERVE*

ITS SIGNIFICANCE IN VOCAL CORD PARALYSIS

CARNES WEEKS, M D, AND J WILLIAM HINTON, M D

NEW YORK, N Y

VOCAL CORD PARALYSIS, if it is unilateral, is a serious complication of thyroid surgery and, if bilateral, constitutes a surgical calamity. The patient is generally told after a unilateral cord injury that the voice will return and no treatment is necessary. In the bilateral cord injuries, if the cords are in adduction, a tracheotomy may have to be performed as a life-saving measure, and efforts made at a later date to restore the function of the cords. This may be attempted by some plastic procedure on the cords or else by exposing the recurrent laryngeal nerve with an attempt at anastomosing the severed ends, as advocated by Lahey and Hoover,¹⁰ or anastomosing the distal end of the recurrent laryngeal to the descending branch of the hypoglossal nerve, as advocated by Frazier.⁵

During the past three years, in the Thyroid Clinic at Post-Graduate Hospital, our interest has been aroused by a conservative method of treatment in vocal cord paralysis that was instituted by Dr. Charles O. Fietz, of the Neurologic Department. Lahey and Hoover,¹⁰ in 1938, advised exploring the neck of patients with vocal cord paralysis within the first three months of the operative injury. They felt that if the patient had gone longer than three months there was a greatly diminished chance of nerve regeneration and also a chance of fixation of the arytenoid muscles due to atrophy and fibrosis. Jackson,⁷ in 1937, states that a vocal cord paralysis of six months duration is permanent and can never be restored. With such opinions one would look with skepticism upon any method of conservative treatment being employed to restore a vocal cord that has been functionless for many months. While discussing, in our clinic, the advisability of exploring the neck of a patient with a vocal cord injury which had gone approximately one year, the conservative treatment, as referred to in this presentation, was advised by Doctor Fietz. The optimum time for resuturing the nerve had long since past, according to the teaching of Lahey and Hoover, and the cord was permanently paralysed, by Jackson's concept of vocal cord paralysis. In view of their opinions we felt that conservative treatment would do no harm, and one of the patients whom we present this evening illustrated our first experience with galvanic and faradic stimulation, as carried out by Doctor Fietz with the aid of Dr. A. F. Laszlo, of the Otolaryngology Department. A detailed discussion of the exact technic is being presented before the New York Neurological Society by Doctor Fietz. It will suffice in this presentation to say the nerve is stimulated by an uninterrupted cathode application and the

* Read before the New York Surgical Society April 8, 1942

muscles of the vocal cords by faradic and galvanic stimuli. If the vocal cord does not respond to the faradic and galvanic stimuli on the first examination the prognosis for ultimate improvement is poor, but not necessarily hopeless. Even if no response is elicited on the first examination, treatment is rendered for six weeks and if after that time no response is obtained the nerve is considered permanently injured. A very small percentage of this group will respond to treatment. The favorable cases are those showing movement in the vocal cords to faradic and galvanic stimulation on the first visit, which indicates the motor activity is not completely lost.

We have had occasion to refer 19 patients for electrical treatment during the years 1940 and 1941. It should be stated that all these nerve injuries were by no means incurred at Post-Graduate Hospital, but we can also add that the percentage of injuries occurring after operations performed by the General Surgical Staff far exceeded 3 per cent. This figure, given by Lahey and Hoover,¹⁰ was the average, and was high compared to their clinic, 1.6 per cent before demonstrating the recurrent laryngeal nerve, and 0.3 per cent after demonstrating the recurrent laryngeal nerve at operation.

After we had seen definite clinical improvement in vocal cord paralysis following the electrical stimulation, the problem was discussed by the authors, and we felt the explanation of the clinical improvement was due to incomplete loss of the motor activity of the recurrent laryngeal nerve, that many nerves had two branches, one branch would be injured while the other remained intact. The intact branch was so reduced as to represent one-third or one-half the original caliber of the nerve and, therefore, only able to function when assisted by artificial stimulation to regain motor control over the injured muscles. Therefore, we wish to report our findings on a group of dissections, made in the Anatomical Laboratory at Post-Graduate Hospital, which were undertaken by the authors, and consisted of ten cadavers, and the exposure of 19 nerves (Tables I and II). We wish to report the ob-

TABLE I
POST-GRADUATE HOSPITAL SERIES
Weeks and Hinton
Ten Cadavers—19 Nerves
78 Per Cent Divided Extralaryngeally

RIGHT SIDE					
Division of Nerve	Extralaryngeal Division in Cm	Division in Relation to Thyroid Gland	Relation of Nerve to Inferior Thyroid Artery	Relative Diameter of Divisions	
Two	4 cm	Lower pole	Posterior	65%—35%	
Two	2 cm	Middle third	Posterior	75%—25%	
Single*			Anterior		
Two	2.5 cm	Lower pole	Anterior	65%—35%	
Two	1 cm	Upper third	Anterior	50%—50%	
Two	2.5 cm	Middle third	Anterior	65%—35%	
Three	2 cm	Middle third	Anterior	50%—25%—25%	
Two	2.5 cm	Lower third	Posterior	75%—25%	
Two	3 cm	Lower pole	Anterior	50%—50%	

* Single Between branches of inferior thyroid artery

VOCAL CORD PARALYSIS

TABLE II
POST-GRADUATE HOSPITAL SERIES
Weeks and Hinton
Ten Cadavers—19 Nerves
78 Per Cent Divided Extralaryngeally

LEFT SIDE				
Division of Nerve	Extralaryngeal Division in Cm	Division in Relation to Thyroid Gland	Relation of Nerve to Inferior Thyroid Artery	Relative Diameter of Divisions
Two	4 cm	Lower pole	Posterior	65%—35%
Two	5 cm	Lower pole	Posterior	65%—35%
Single*			Anterior	
Destroyed				
Two	1 cm	Upper third	Anterior	50%—50%
Two	2.5 cm	Middle third	Anterior	50%—50%
Two	2.5 cm	Middle third	Posterior	50%—50%
Two	3 cm	Lower pole	Posterior	50%—50%
Two	3 cm	Middle third	Anterior	50%—50%

* Single Between branches of inferior thyroid artery

servations made in the Anatomical Laboratory of New York University by Mr. John Stewart and Mr. Roger Moore, who are fourth year medical students. They did this as a favor to the authors, checking our observations on 18 cadavers, with 24 nerve exposures (Tables III and IV). In the dis-

TABLE III
NEW YORK UNIVERSITY SERIES
Stewart and Moore
Eighteen Cadavers—24 Nerves
78 Per Cent Divided Extralaryngeally

RIGHT SIDE				
Division of Nerve	Extralaryngeal Division in Cm	Division in Relation to Thyroid Gland	Relation of Nerve to Inferior Thyroid Artery	Relative Diameter of Divisions
Two	2.2 cm	Lower third	Anterior	65%—35%
One			Anterior	
Two	1.5 cm	Middle third	Anterior	50%—50%
Single			Anterior	
Destroyed				
Two	2.0 cm	Junction of middle and lower third	Posterior	50%—50%
Destroyed				
Destroyed				
Single			Posterior	
Destroyed				
Two	2 cm	Junction of middle and lower third		75%—25%
Destroyed				
Two	2.5 cm	Lower third	Anterior	65%—35%
Two	2.0—2.0 cm	Middle third	Posterior	65%—35%
Two	3.5—2.5 cm	Lower pole	Posterior	65%—35%
Destroyed				
Destroyed				
Destroyed				

sections at Post-Graduate Hospital we found that 78 per cent of the recurrent laryngeal nerves divided extralaryngeally while at New York University it was the same. Many of these nerves started their division at the level of the lower pole of the gland. These findings would, obviously, explain how

it is possible to injure one extralaryngeal branch at operation, with complete paralysis of the vocal cord on the corresponding side, and making it possible for electrical stimulation to restore the cord to a state of functioning after a

TABLE IV
NEW YORK UNIVERSITY SERIES
Stewart and Moore
Lighten Cadavers—24 Nerves
75 Per Cent Divided Extralaryngeally

LEFT SIDE				
Division of Nerve	Extralaryngeal Division in Cm	Division in Relation to Thyroid Gland	Relation of Nerve to Inferior Thyroid Artery	Relative Diameter of Divisions
Two	1.6 cm	Lower third	Anterior	65%—35%
Two	3.0 cm	Inferior pole	?	50%—50%
		Junction of middle and lower third	Posterior	50%—50%
Single			Anterior	
Two	1.0 cm	Middle upper half	?	65%—35%
Destroyed				
Two	1.25 cm	Middle third	Posterior	65%—35%
Two	2.0 cm	Inferior pole	Artery splits the 2 branches	50%—50%
Destroyed				
Two	2.0 cm	Junction of middle and lower third	Posterior	50%—50%
Two	2.5 cm	Inferior pole	Artery splits branches of nerve	75%—25%
Two	1.5 cm	Middle third	Posterior	65%—35%
Single			Anterior	
Destroyed				
Two	2.25 cm	Inferior pole	Posterior	50%—50%
Three	2.5 cm	Inferior pole	Posterior	40%—20%
Single			Posterior	
Two	2.0 cm	Middle and lower third	Posterior	50%—50%

definite period of paralysis, meaning one that has existed in terms of years rather than in terms of months. Figure 1 is an actual photograph from a dissection showing the nerve dividing with one branch 65 per cent, and the other 35 per cent of the original caliber of the nerve.

When one reviews the anatomy of the recurrent laryngeal nerve, and recent articles which include numbers of dissections of the laryngeal nerve, one wonders why this point has not been stressed before. In all probability the nerves were not completely dissected as they entered the larynx at the inferior horn of the thyroid cartilage. The authors had other points of interest in their dissections, for instance, one point of controversy has been the position the recurrent laryngeal nerve had in relation to the inferior thyroid artery. Although several articles have been published to clarify this point, after anatomic dissections, there is considerable difference of opinion. Fowler and Hanson,⁶ in a very excellent article on 200 dissections, state that in 65.5 per cent the nerve was posterior to the artery, and in 26 per cent anterior, and in 8.5 per cent it lay between the branches. Berlin and Lahey,⁷ in 22 dissections, state the nerve is anterior to the artery in 18 cases on the right side, and posterior to the artery in 19 cases on the left side. Ziegelman,¹¹

in 42 dissections, reports the nerve anterior to the artery in 17, and posterior to the artery in 12, and between in 13, while our own dissections essentially confirm those of Ziegelman. There have been three references made in the literature to the nerve having extralaryngeal branches. Berlin¹ reports two instances, in 70 total thyroidectomies, where the recurrent laryngeal nerve branches at the inferior pole of the gland, and in one instance the anterior branch was divided, with paralysis of the vocal cord on the same side. Nord-



FIG. 1.—Photograph showing division of recurrent laryngeal nerve at the lower third of gland. Branches 65.35 per cent of the original caliber.

land,¹¹ in 31 cadavers, found in two instances branches between the inferior thyroid artery on the left side, and in two instances branches between the inferior thyroid artery on both sides. Lahey,⁹ in an article advocating the dissection of the recurrent laryngeal nerve in subtotal thyroidectomies, has an illustration in which the recurrent laryngeal nerve branches extralaryngeally, and says that he has repeatedly seen the extralaryngeal division of the nerve in the course of dissecting the nerve during thyroidectomies which at that time had numbered over 3,000 cases.

How easily the recurrent laryngeal nerve is injured by handling or manipulation of the gland, or by traction, is important. If it is easily injured then one would have a logical explanation of why a nerve would refunction after months, or perhaps years, with the aid of electric stimulation. Crile⁴ as recently as 12 years ago, stated that the slightest direct or indirect pressure on the recurrent laryngeal nerve interfered with nerve conduction and immediately changed the voice. Doctor Fietz feels as Crile did, and doubts our anatomic explanation of the clinical improvement. The experimental work of Judd, New and Mann⁸ contradicts this in their work on dogs, they put traction on the nerve, several times greater than one would use in performing a thyroidectomy, without producing any voice changes. Lahey,⁹ more recently, has confirmed the observations of Judd, *et al* and states, in

over 3,000 dissections, he does not believe the nerve was injured by handling during such a procedure

It is important to stress the motor function of the superior laryngeal nerve as causing voice change in thyroid operations. It is a well-known fact that the external branches of the superior laryngeal nerve, which accompanies the superior artery, supply the cricothyroid muscle. The cricothyroid muscle is a tensor muscle of the larynx, and its paralysis results in a hoarseness or a voice that becomes tired after moderate talking. The internal branch of the superior laryngeal nerve also has a definite motor function, and supplies the arytenoids which are adductors in function. Nordland,¹¹ in 19 laryngeal dissections, found the arytenoid muscles were supplied by the internal branch of the superior laryngeal nerve in 18 specimens, and in one specimen a branch of the recurrent laryngeal nerve and the internal branch of the superior laryngeal supply the arytenoid muscles.

The percentage of vocal cord paralysis in unoperated goiters is one of extreme interest, particularly when the postoperative incidence is given in the literature as only from 0.3 to 3 per cent by different authors. The preoperative paralysis, which one assumes is due to pressure on the nerve, is given as 5 to 10 per cent by Wolfe¹, who is quoted by Reinhoff.¹² If so, preoperative examination of the vocal cords in all goiter patients is essential. Obviously, any patient who has had a thyroid operation of any kind should have the vocal cords examined, even though the operation has been inferior or superior pole ligation. In our clinic we have not encountered any preoperative vocal cord paralysis in unoperated cases. Lahey⁸ has stated that the routine laryngeal examination in unoperated cases is such a burden, and *so seldom of any clinical significance, that he has stopped doing it routinely*. That does not mean that in case of a large goiter that produces pressure symptoms, the patient should not have preoperative vocal cord examination, but in the hyperplastic goiter and small nodular goiter it seems of very little value. One should remember that Wolfe's statement for preoperative injury to the vocal cords was made in 1879, and he was observing large goiters, and many of them were substernal.

The point at which the nerve is usually injured is generally agreed to be at its entrance into the larynx in the region of the inferior horn of the thyroid cartilage. This site has been stressed by Blalock and Crowe,³ and our clinical observations confirm their statement. That being the case, one can readily see how difficult it is to prevent injury to one of the branches of the recurrent laryngeal nerve by exposing the nerve at the inferior thyroid artery, unless the nerve is completely dissected free and the dissection carried to the larynx, thus making sure that both branches are visualized. This is, anatomically, rather difficult with the thyroid gland in place. Therefore, one might question the wisdom of dissecting the recurrent laryngeal nerve as a routine operative procedure. The extralaryngeal division of the recurrent laryngeal nerve, in a high percentage of anatomic dissections, can explain

the favorable results in many of our cases and can also explain why, in a definite percentage of cases, failure to improve will be encountered due to the fact that the nerve has no extralaryngeal branches

COMMENT

The conservative treatment for vocal cord paralysis, that has been discussed in this presentation, seems to have a definite anatomic basis, and a certain degree of success should be anticipated from such a procedure. In 19 cases there were two bilateral paralyses from roentgenotherapy. One of these patients had worn a tracheotomy tube for seven years before treatment was instituted. Within three months after instituting treatment the tracheotomy tube was removed, and the patient has a normal voice, as was seen from the case presented this evening. The other patient had gone three years before treatment was started and she has a normal voice at the present time. These cases fall in a different category from operative injuries.

The mechanism is an ankylosis of the cricoarytenoid joint, due to the severe inflammatory reaction from the roentgenotherapy. There were six bilateral and 11 unilateral operative cases. Of the six bilateral, two were complete failures, three were greatly improved and one was cured. Of the 11 unilateral injuries, two were cured, four were greatly improved, and five were definitely benefited.

From our case presentations it would seem there is a definite place for conservative treatment of vocal cord paralysis, as rendered by Doctor Fiertz. In those cases with an extralaryngeal division of the recurrent laryngeal nerve, if the impulses have not been completely interrupted, a cure, in the sense of a normal functioning vocal cord, can be anticipated in a certain percentage of operative injuries.

A vocal cord paralysis that has existed beyond the six months' period does not represent a permanent paralysis, as stated by Jackson, according to our observations in the above 19 cases.

REFERENCES

- ¹ Berlin, D. D. Recurrent Laryngeal Nerves in Total Ablation of the Normal Thyroid Gland. Anatomical and Surgical Study. *Surg., Gynec. and Obstet.*, **60**, 19-26, January, 1935.
- ² Berlin, D. D., and Lahey, F. H. Dissection of the Recurrent and Superior Laryngeal Nerves. *Surg., Gynec. and Obstet.*, **49**, 102-104, July, 1929.
- ³ Blalock, A., and Crowe, S. J. The Recurrent Laryngeal Nerve in Dogs. Experimental Studies. *Arch. Surg.*, **12**, 95-116, 1925.
- ⁴ Crile, W. J. The Prevention of Abductor Paralysis in Thyroidectomy. *Surg., Gynec. and Obstet.*, **49**, No. 4, October, 1929.
- ⁵ Frazier, C. H. Treatment of Paralysis of the Recurrent Laryngeal Nerve by Nerve Anastomosis. *ANNALS OF SURGERY*, **79**, 161, February, 1924.
- ⁶ Fowler, C. H., and Hanson, W. A. Surgical Anatomy of the Thyroid Gland. With Special Reference to the Relations of the Recurrent Laryngeal Nerve. *Surg., Gynec. and Obstet.*, **49**, 59-65, July, 1929.
- ⁷ Jackson, C., and Jackson, C. L. The Larynx and Its Diseases. W. B. Saunders and Co., p. 294, 1937.

- ⁸ Judd, E S , New, G B , and Mann, F C The Effect of Trauma upon the Laryngeal Nerves An Experimental Study ANNALS OF SURGERY, 67, 257-262, March, 1918
- ⁹ Lahey, F H Operative Injury to Recurrent Nerve Surg Clin North America, 12, 839-848, June, 1932
- ¹⁰ Lahey, F H, and Hoovei, W B Injuries to the Recurrent Laryngeal Nerve in Thyroid Operations Their Management and Avoidance ANNALS OF SURGERY, 108, 545-562, October, 1938
- ¹¹ Nordland, M The Larynx as Related to Surgery of the Thyroid An Anatomic Study Surg, Gynec, and Obstet, 51, 449-459, October, 1930
- ¹² Reinhoff, Wm F, Jr Lewis' Practice of Surgery, Vol 6, Chapter 1, p 145, 1940
- ¹³ Ziegelman, E F Laryngeal Nerves Surgical Importance in Relation to Thyroid Arteries, Thyroid Gland and Larynx Arch Otolaryng, 18, 793-808, December 1933

REPAIR OF DIRECT INGUINAL HERNIA WITH OSTEOPERIOSTEAL TRANSPLANT

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ONE out of every five direct inguinal herniae operated upon has recurred. This high percentage of surgical failures has not gone unchallenged. Many original procedures and modifications of the old ones have been tried, but none of these have materially reduced the number of recurrences. The excellence attained in the surgery of indirect inguinal herniae can be traced to the successful anatomic reconstruction of the defect in the abdominal wall. The failure to achieve comparable success in the direct type must be attributed to the incomplete reconstruction of the defect in the abdominal wall. In 1938, Veal and Baker¹ described an operation for direct hernia based upon the construction of a new floor of Hesselbach's triangle with an osteoperiosteal transplant. The results obtained with this new procedure in 85 cases have been so encouraging that I feel a follow-up report is now warranted.

In order to make clear the principle of the osteoperiosteal repair it is necessary to review the normal anatomy of the structures involved, and show how these structures are altered when a direct hernia develops. A direct hernia pierces the abdominal wall through Hesselbach's triangle. This triangle is bounded laterally by the deep inferior epigastric vessels, medially by the edge of the rectus muscle, and inferiorly by the inguinal ligament. These boundaries are of little importance except for the point of diagnosis. The structures forming the floor of this triangle are most important because a hernia cannot develop if they are normally formed and remain intact. The floor of Hesselbach's triangle is made up of several layers. From within outward are the peritoneum, extraperitoneal fat, transversalis fascia, and the conjoint tendon. The peritoneum should not be considered as a buffer. The transversalis fascia is a thin aponeurotic membrane which lies between the inner surface of the transversus abdominis muscle and the extraperitoneal fat. In the inguinal region it becomes closely adherent to the aponeurosis of the transversus. The conjoint tendon is a thick, inelastic fibrous sheet which forms a solid barrier in the floor of the Hesselbach's triangle. This tendon is formed by the union of the tendons of the obliquus internus and transversus abdominis muscles. The tendinous portions of these muscles become fused and continue as a single broad sheet medially toward the rectus sheath and downward toward the pubis. It is inserted into the rectus sheath, the crest of the pubis, and the ascending ramus of the pubis. Its attachment to the ascending ramus is along the pectineal line and extends laterally to the deep inferior epigastric vessels (Fig 1). The conjoint tendon is also loosely joined to the inguinal ligament, but this is not a true anatomic insertion.

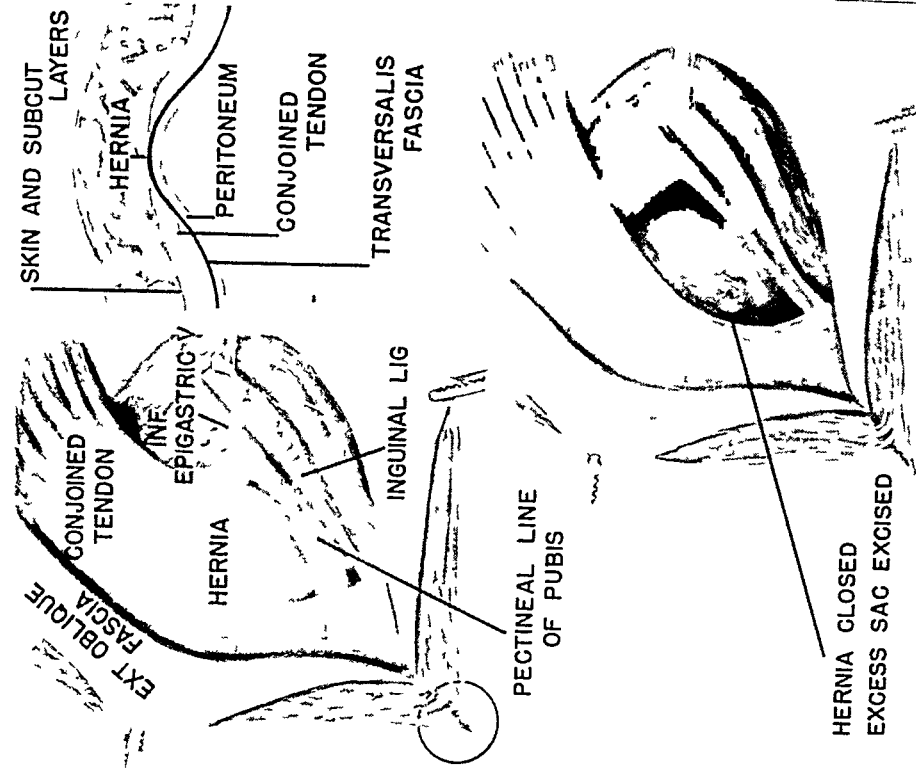


Fig 2.—Drawing showing the development of a direct hernia and its relations to the pectineal line of the pubis. Note the defect through Hesselbach's triangle after the sac has been ligated

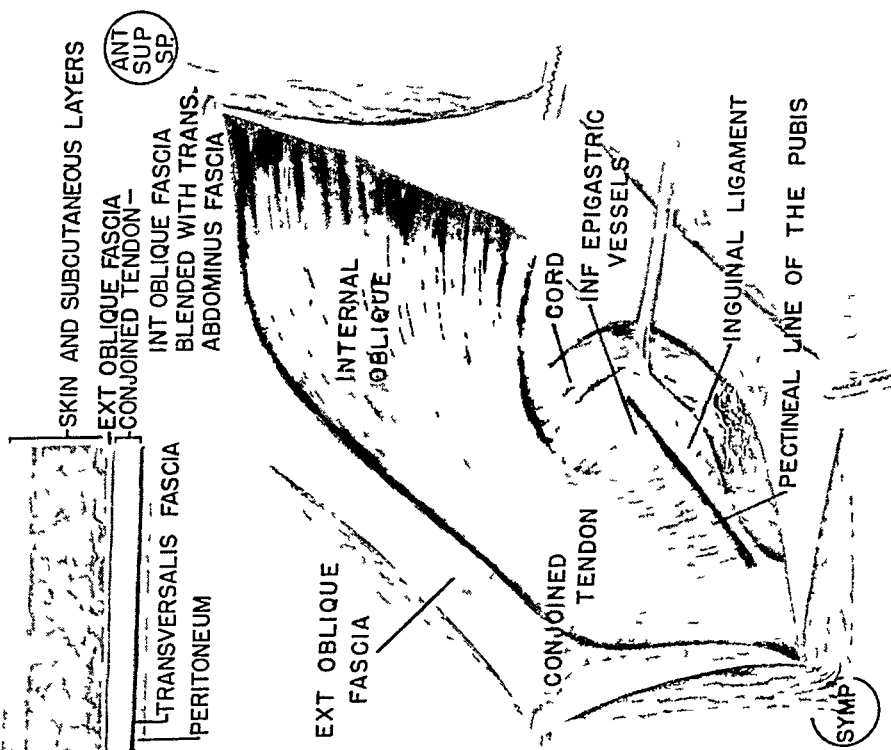


Fig 1.—Drawing showing the normal relations and attachments of the conjoined tendon

A hernia may occur if there is a short attachment of the tendon along the pectineal line. This leaves a point of natural weakness just medial to the deep inferior epigastric vessels. After years of stress and strain the peritoneum and transversalis fascia may push forward through this weak spot. By continued stretching the conjoined tendon is worn away and a true direct hernia develops. By the same process an indirect hernia may gradually encroach upon and displace the attachment of the conjoined tendon and a combination direct and indirect hernia is formed. In both of these types the true transversalis fascia is stretched in front of the protruding peritoneum and may form part of the covering of the hernia. If the hernia becomes very large the transversalis may be destroyed over the dome of the sac. The majority of direct herniae result from prolonged stretching and thinning-out of that portion of the conjoined tendon extending from the edge of Gimbernat's ligament to the margin of the deep inferior epigastric vessels (Fig. 2). In this type the conjoined tendon may be completely separated from its attachment to the pubis. In other cases it may remain partly attached. As in the first type the transversalis fascia frequently is simply stretched in front of the peritoneum and forms one of the layers of the covering of the hernia. Occasionally a hernia develops through a longitudinal split in the conjoined tendon. Regardless of the mode of development, the important alteration in the anatomy is the disintegration of that part of the conjoined tendon that is normally attached to the pectineal line of the pubis.

If there is to be an anatomic repair of a direct hernia the operation must include the reconstruction of the damaged conjoined tendon and the restoration of its insertion into the pubis. Direct attempts to repair the damaged tendon and to reestablish its attachment fail except in the case of a very small defect. The hernia usually produces a wide gap in the abdominal wall between the intact portion of the tendon and the superior ramus of the pubis. The inelastic character of the tendon makes it impossible to reunite this structure to its normal place of insertion. The operations of Wolfer, Bloodgood, Halsted, Hotchkiss, Lusk, Beigel, and Downes all aim to create a buffer in front of the defect in the floor of Hesselbach's triangle. None have materially reduced the recurrence rate of direct herniae.

In order to accomplish a reconstruction of the floor of Hesselbach's triangle a substitution of the destroyed structure must be made. In search for some suitable "substitute tissue" my attention was turned to the study of the ultimate fate of various types of autogenous grafts. From the excellent communications by MacEwen,² and Gallie and Robertson,³ it would appear that an osteoperiosteal transplant applied to bone or periosteum becomes firmly united to those structures through the formation of fibrous tissue. Furthermore, when periosteum, bone and periosteum, or bone alone is transplanted into tissue where they are not normally found, or where there is no function for them to perform, they are replaced by dense fibrous tissue scar. In a series of experiments upon dogs I found that when free osteoperiosteal grafts were attached to the transverse processes of the spinal vertebrae and to the spinal

muscles they became absorbed within a few weeks. However, there had been left a thick, dense layer of fibrous tissue firmly united to the muscles and the transverse processes. It was also found that bone and periosteum was more fibrogenetic than periosteum alone. It seemed then that an osteoperiosteal transplant would answer the purpose for the "substitute tissue" with which to reconstruct the floor of the Hesselbach's triangle. Upon the basis of these observations and from the consideration of the pathologic anatomy of a direct inguinal hernia, the new principle which I now employ was developed. Since the preliminary report of the operation was published certain changes have been made. Therefore, I wish to describe in more detail the technic of the procedure in this communication.

Technic of the Operation—The lower abdomen, including the inguinal region, is prepared in the usual manner. One leg is also prepared from the knee to the ankle. The sterile drapes are so placed that both fields are exposed. Since this operation entails two distinct procedures in two unrelated parts of the body teamwork is essential. The plan has been for one surgeon to devote his attention to the inguinal region while his assistant removes the osteoperiosteal graft from the anterior surface of the tibia. In order to follow the operation in steps the preparation of the graft will be described first.

The Osteoperiosteal Transplant—An incision about eight inches in length, beginning at the level of the tibial tubercle, is made over the anterior surface of the tibia. The skin is reflected, thereby exposing the periosteum covering the broad anterior surface of the bone. The periosteum to be removed is outlined with the point of the scalpel. Its shape is somewhat like that of a tennis racquet, the oval part being the head piece and the handle forming the tail portion (Fig. 3). The size of the head piece is determined by the width of the defect produced by the hernia as it protrudes through the floor of Hesselbach's triangle. It must be wide enough to completely bridge this defect. It is cut from the enlarged upper end of the tibia. The tail piece is simply the prolonged tapering portion of the graft, and is about six inches in length. After the graft has been outlined on the tibia the periosteum is divided about its entire course (Fig. 3). The head piece is elevated with a chisel by cutting thin slivers of bone from the tibia, and leaving them attached to the periosteum. When the tail portion is reached the periosteum is simply elevated from its bed. The graft then consists of an oval shaped head piece of periosteum covered with slivers of bone and a thin tail portion of free periosteum. After the graft has been removed the incision is closed by bringing the skin edges in apposition with interrupted silk sutures. It is not necessary to attempt to close the periosteal bed.

Technic of Hernioplasty—An oblique incision is made over the inguinal canal. The external oblique fascia is divided and the cord and hernia are exposed. The cord is retracted laterally, and the exact nature of the hernia is determined. The size of the defect in the floor of Hesselbach's triangle is noted. The sac is then picked up in forceps and incised at its apex. A purse-string suture is placed around its base and the excess portion is excised. The

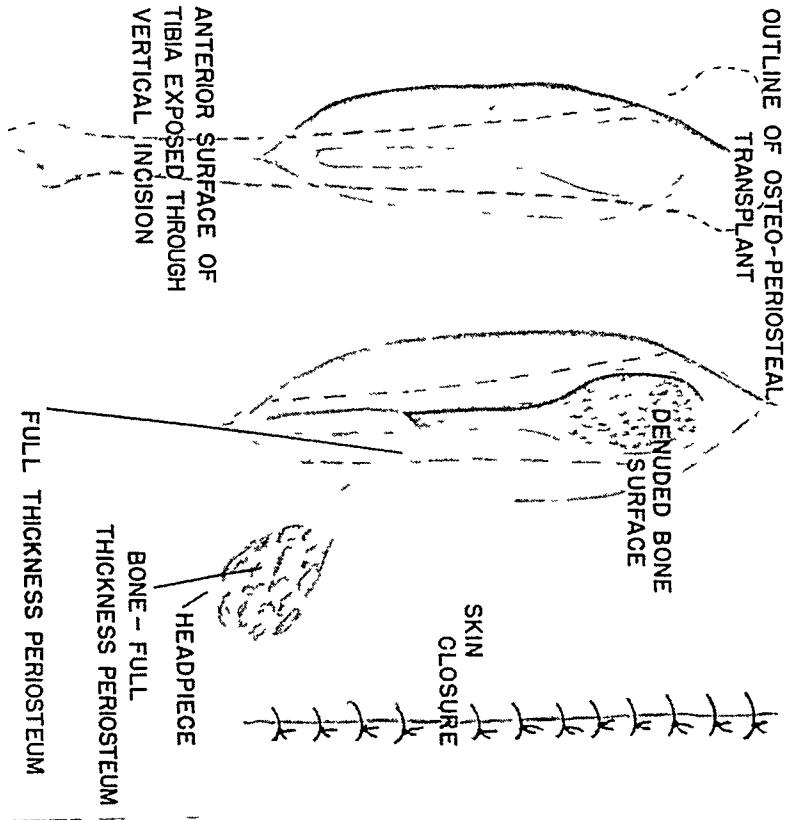


Fig. 3—Drawings showing the removal of osteoperiosteal graft from the tibia. Note that the head piece of the graft contains bone and full thickness periosteum. The tail piece is only periosteum.

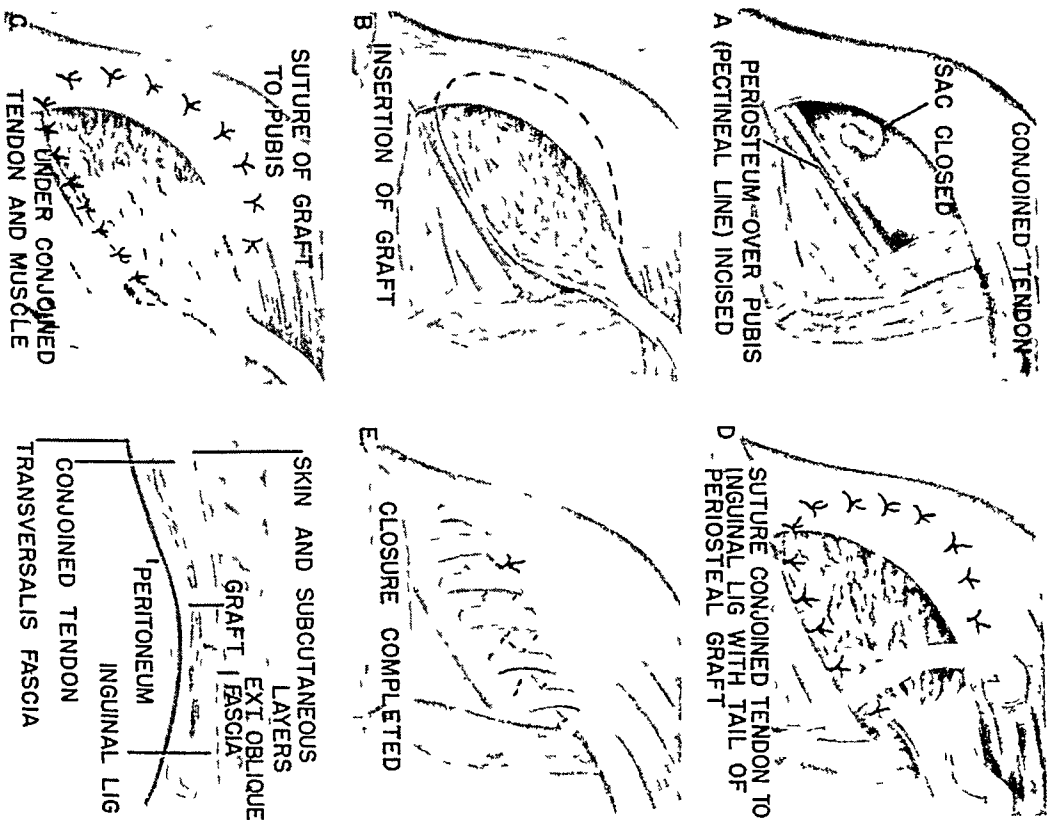


Fig. 4—Drawings showing technique of repair of the anatomic defect in the conjoined tendon in a direct inguinal hernia. Note that the bone surface of the graft is turned outward. Note also the use of the tail piece as a fascial suture.

inferior epigastric vessels are identified. The conjoined tendon is freed from all areola tissue and fat along its free edge. The ligated sac is then pushed away from the pubis by gentle finger dissection. The periosteum just posteriorly to the pectineal line of the pubis is incised from the lateral edge of the Gimbernat's ligament to the margin of the inferior epigastric vessels (Fig 4). If these vessels seem to interfere with the closure they are ligated and divided. The field is now ready for the reception of the graft. The head piece of the transplant, with bone surface upward, is placed in the gap between the pectineal line of the pubis and the conjoined tendon (Fig 4). The inferior margin of the transplant is sutured into the slit in the periosteum of the pubis with interrupted silk sutures. The superior margin of the transplant is placed posterior to the conjoined tendon and sutured to that structure with interrupted silk sutures. These sutures extend from the angle at Gimbernat's ligament to the edge of the tail of the transplant. This portion of the transplant is now utilized to approximate the free margin of the inferior border of the conjoined tendon to the inguinal ligament after the manner used for the Gallie-type of fascial suture. The first suture is passed through conjoined muscle, just above the beginning of the tendon, then down through the inguinal ligament (Fig 4). From this point the suture is woven back-and-forth from the conjoined tendon to the inguinal ligament until these structures are approximated from the inferior epigastric vessels to Gimbernat's ligament. A final silk suture is used to fix the end of the transplant into the tendon. The cut edges of the external oblique fascia are closed behind the cord. The cord is now placed in its new bed and the subcutaneous tissues and skin closed in the usual manner.

The first operation using this new principle was performed in February 1937, at Charity Hospital, New Orleans. During the following 16 months 20 additional such repairs were performed at the same institution. All of the cases were carefully followed—14 for a period of six months to one year. There was not a single recurrence. In July, 1938, I came to Gallinger Municipal Hospital, Washington, D. C., and have lost contact with the Charity Hospital cases. My associates and I have performed the same operation upon 64 patients at the Gallinger Hospital, and have succeeded in following all of these by personal observation. In 34 cases the follow-up period ranges from one year to two and one-half years. Six months to one year has elapsed since operation upon 20 additional patients. Including the Charity Hospital group, there are now 68 cases in which the follow-up period has been at least six months. In the entire series of 85 cases there has been only one recurrence. This failure was the direct result of a gross infection of the wound. It occurred early in the postoperative period and the entire graft was eventually extruded.

The postoperative care of these cases has been the same as for all inguinal herniae. The patient is allowed out of bed on the fourteenth day. He may resume his usual occupation eight weeks following his operation. The healing process seems to be just as rapid as that following the simple Bassini operation. There is one great difference noted in the osteoperiosteal repairs—the recon-

structed wall is thicker and more rigid. Even in the cases with the longest follow-up period there still remains a strong inguinal wall, which is firmly united to the pubis. This obvious building-up of a new fibrous wall has not been attended by any discoverable ill effects. Since the cord is transplanted outside the fascial layers there has been no damage to this structure. The osseous portion of the transplant is gradually absorbed. It has been possible to follow this process by means of repeated roentgenologic studies. The first roentgenogram, made during the early days of the convalescent period, has shown the outline of the bone in the graft merging into the denser shadow of the pubis along the line of the attachment. Roentgenograms made six weeks later failed to show this shadow in some, but it was still present in others. In all the cases studied there has apparently been a complete absorption of the bone within three months.

There have been three wound infections, two of these involving all layers, the other being only superficial. In one of the grossly infected wounds, the slivers of bone contained in the graft were gradually sloughed, but there has been no recurrence of the hernia two years after the original repair. In the other grossly infected wound the entire graft was extruded within two weeks after the repair, and there was an immediate recurrence of the hernia. The leg wound has healed in all cases by primary union. There has been no evidence of any damage to the tibia. In one case an hematoma developed under the skin and had to be evacuated, but no serious consequences followed.

Although the number of cases included in this report is small, and the follow-up period inadequate, certain conclusions can be drawn. A clear understanding of the pathologic anatomy of a direct hernia is essential. The operation does not require any special equipment or any unusual postoperative care. The removal of the osteoperiosteal graft from the tibia has not caused any disability or prolonged the convalescent period. The results of the operations usually employed for direct hernia show that about one-half of the recurrences develop within six months. In the present series, 68 consecutive cases repaired with the osteoperiosteal transplant have remained intact over a six-month period. This seems to indicate that the anatomic defect has been successfully bridged. The permanency of the repair can be determined only by a much longer follow-up study.

REFERENCES

- ¹ Veal, J. Ross, and Baker, Dan D. Repair of Direct Inguinal Hernia by Osteoperiosteal Graft to the Pectineal Line of the Pubis. *Surgery*, 3, 585-592, April, 1938.
- ² MacEwen, W. The Growth of Bone. Glasgow, James Maclehose and Sons, 1912.
- ³ Gallie, E. W., and Robertson, D. E. The Repair of Bone. *Brit Jour Surg*, 7, 211-261, 1919-1920.
- ⁴ Watson, L. Hernia. St. Louis, C. V. Mosby Co., 1924.

UNUSUAL VISCERA IN INDIRECT INGUINAL HERNIAE

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THE PRESENCE OF AN OVARY in the sac of an inguinal hernia is not common, most surgeons of large experience having encountered it one or more times. However, the presence of the uterus in an indirect inguinal hernia is rare. The earliest report of an inguinal hysterocele was made by Nicholas Pol, in 1531. While it is not stated, this was undoubtedly a direct type of hernia. Seneitius and Hildarus, in 1610 reported a case which they claimed was identical to the one described by Pol. Another case described by these authors, and which was attributed to Doringuis, is variously classified as ciural or inguinal. Study of these early reports shows that considerable confusion existed both as to the authenticity and exact nature of these cases.

Watson collected from the literature 30 cases of hysterocele, and 61 cases of hernia of the nonpregnant uterus—a total of 91, 219 cases of hernia of the adnexa, 80 cases of tubal hernia, and 181 cases of the ovary alone.

While it is impossible to give the exact percentage of incidence of this complication, it can be readily seen that it would be very small considering the number of herniotomies performed.

Few of the cases reported are accurately described as to whether they are direct or indirect inguinal herniae. For example, Jobson, in 1904, and Andrews, in 1906, reported hernia of the uterus which was apparently of the direct type. Makkas, in 1910, reported bilateral uterine hernia of a bicornate uterus, and here again a direct hernia existed. Only one author, Ludington, in 1920, definitely recorded a case of the presence of the uterus in an indirect inguinal hernia in a child—age 19 months.

So far as the presence of ovaries and tubes in the sac of an inguinal hernia is concerned, we find in the literature numerous references, the earliest appearing in the writings of Soranus of Ephesus about A. D. 97. McNealy, in 1914, reported a case of strangulated tubo-ovarian hernia in an infant, and, in 1920, a sliding hernia of the fallopian tube. Deutschman, in 1923, reported a case of congenital absence of the vagina associated with bilateral hernia of a uterus bicornate tubes and ovaries. In 1928, Sainoff reported a case of direct hernia of the uterus and tubes through the inguinal canal. Further review of the literature shows a case of direct inguinal hernia containing the ovary, tube and horn of the uterus, reported by Hilarowicz, in 1928. In 1938, Remberger published an interesting study of the human ovo-testis associated with a congenitally bisected uterus herniated into the inguinal canal.

While these cases are rarely encountered, it seems worth while to report them and to call attention again, to such complications arising in the surgical problems of hernia.

CASE REPORTS

Case 1—A white woman, age 30, married, by occupation a professional acrobatic dancer, was admitted to Wesley Memorial Hospital, February 9, 1941, complaining of a lump in the right groin which appeared after a fall at the age of eight years. The lump could be reduced until eight years ago, since which time it has persisted in its

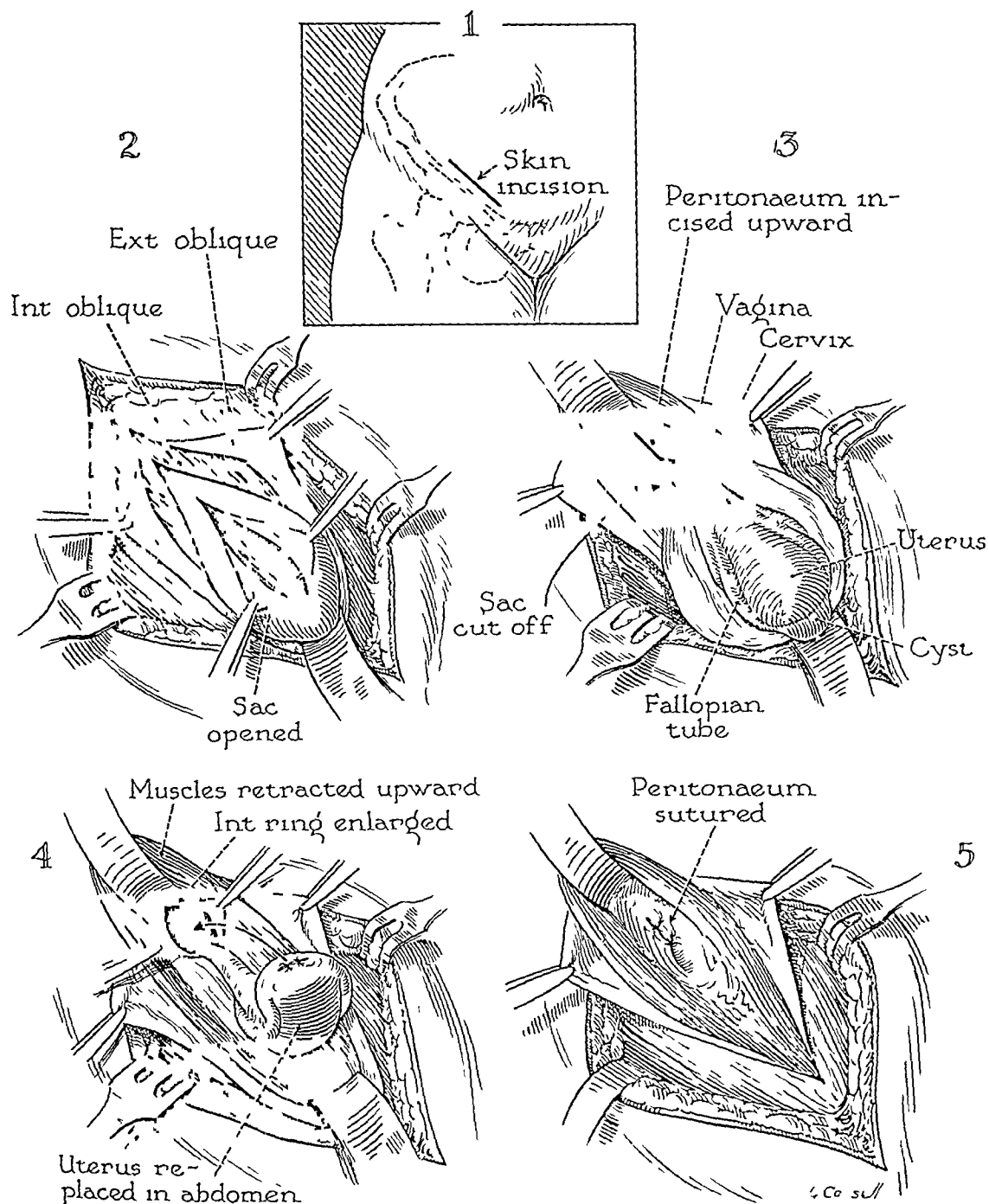


FIG. 1—Sac of the indirect inguinal hernia opened interiorly, showing rudimentary uterus present location. A left inguinal herniorrhaphy had been performed at the age of six. The remainder of her history was essentially negative except that she had never menstruated, and that there was a familial tendency toward hernia, as evidenced by a history of hernia in her grandfather, mother, sister and nephew.

Physical Examination—This revealed entirely negative findings throughout except for the presence in the right groin of a mass the size of a hen's egg which presented

its tip at the external ring, giving rise to an impulse on coughing. Pelvic examination showed the absence of the cervix, the uterus could not be palpated. All secondary sex characteristics were normal.

Operation—Avertin and cyclopropane anesthesia. After exposure of the sac, which was found coming through the internal inguinal ring, it was incised and found to contain a rudimentary uterus which had undergone slight cystic degeneration at the fundus (Fig 1). The cervix could be felt at the base of the sac near the internal ring, although it was necessary, of course, to palpate it through the thickness of the vaginal walls and urinary bladder. The adnexa were not present in the sac. The opening into the abdomen at the neck of the sac would only permit the insertion of the tip of the index finger and it was, therefore, impossible to replace the uterus without enlarging the opening. Due to the failure to find the uterus on bimanual examination prior to operation, the patient had requested that should any abnormal contents of the sac be present she did not wish their removal unless absolutely necessary. The opening into the abdomen was, therefore, enlarged by retracting the muscles upward at the internal ring and incising the peritoneum in the same direction (Fig 1-3). The uterus was then replaced and the usual repair employed after closing the peritoneum.

The patient made an uneventful recovery except for a minor urinary complication, and returned to her work one month after operation.

COMMENT—This case brings up the possibility of the severance of the left round ligament at the time of the first herniotomy at the age of six, since the right hernia appeared two years later, perhaps brought on by her acrobatic activities which she stated commenced in childhood.

Case 2—A white woman, age 29, housewife, married, was admitted to Wesley Memorial Hospital April 10, 1941, complaining of a lump in each groin present since the age of two. These lumps appeared after a fall, and her parents at once applied a truss which she wore until the age of nine. During the last two years she had noticed a pulling sensation associated with some soreness over the swellings, which had first appeared following some corrective exercises.

Her past history was essentially negative except that she had never menstruated. On pelvic examination by a gynecologist some years previously, she was advised that the uterus could not be found.

Physical Examination—This revealed negative findings throughout, except for the presence of two irreducible masses, bilaterally, at the external rings. Pelvic examination revealed the absence of the cervix in the vagina, and the body of the uterus could not be palpated bimanually. All secondary sex characteristics were normal.

Operation—Cyclopropane anesthesia. Exploration of the sac revealed it coming through the internal ring of the left side. Upon opening it, it was found to contain a structure which resembled an undifferentiated gonad the size of a normal testis, accompanied by its vascular supply (Fig 2). The processus vaginalis of this structure was opened, the edges everted and sewed posteriorly to the organ (bottle operation). No communication could be found into the abdominal cavity. Since it is believed by some authorities that extirpation of such structures produces mental changes it was decided to return the gonad to the abdomen after a biopsy specimen was obtained. Accordingly, the muscles were retracted upward at the internal ring and the peritoneum was incised in the same direction, down to the proximal end of the incision in the processus vaginalis. Through this opening an effort was made to locate the uterus, but it could not be found, although the opening was not sufficiently large to be certain. The gonad was then replaced in the abdomen and, after closure of the peritoneum, the usual repair of the hernia was carried out. An incision was then made on the right side. The findings were the same as on the left side, and, consequently, the same technic was employed.

Pathologic Examination—Microscopic Dr E R Strauser "The biopsy specimen consists entirely of fibrous tissue with the exception of some tubular structures which are probably of testicular origin. This cannot be definitely stated because they also resemble embryonic remnants, which are often found about the tubes. I do not believe they belong definitely to either the male or female genitalia."

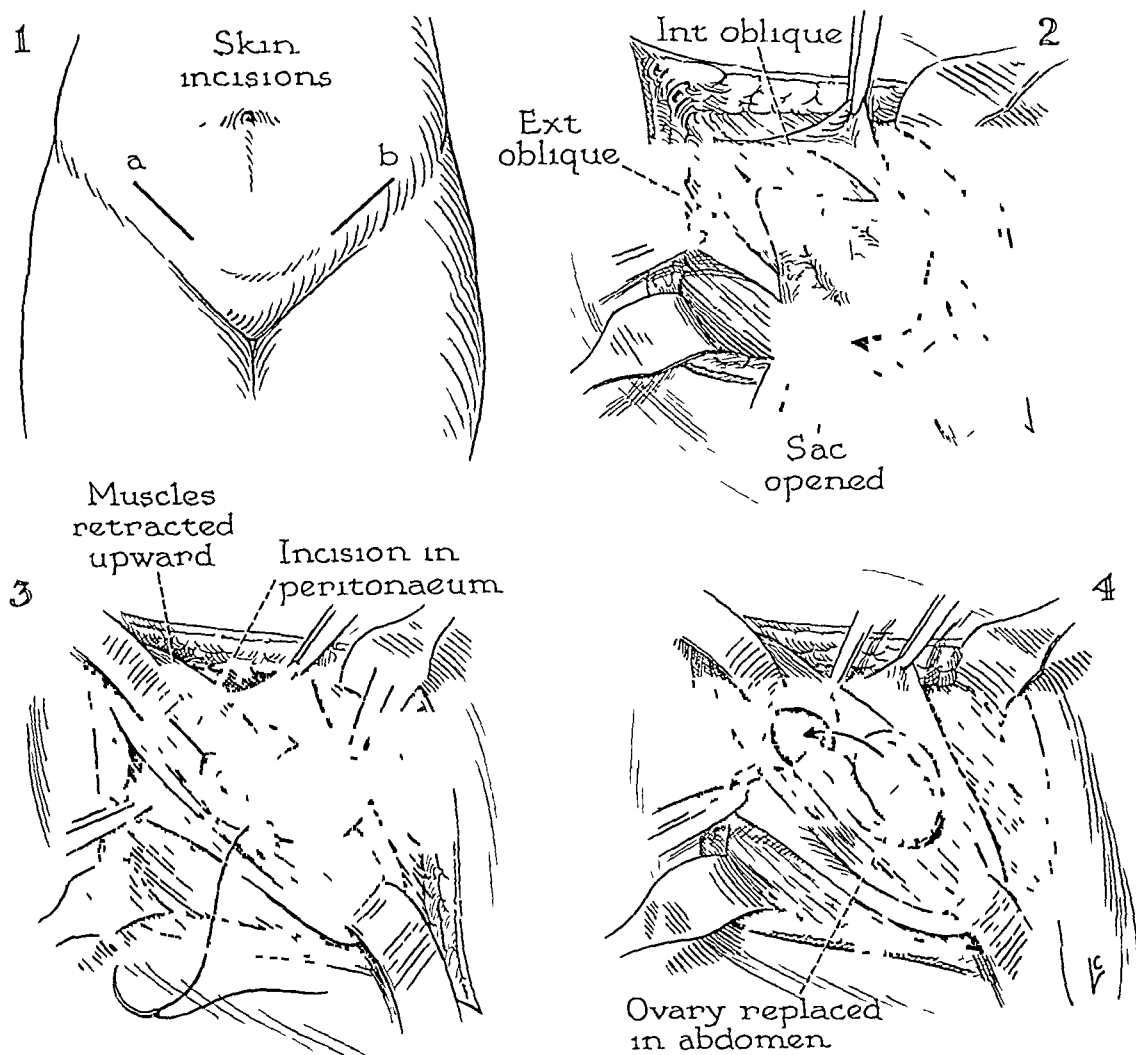


FIG 2—Sac of the right indirect inguinal hernia opened anteriorly, showing the gonad lying midway along the inguinal canal. A similar condition was found on the left side.

CONCLUSIONS

Two cases are reported, one containing the uterus in the sac of an indirect inguinal hernia, and the other, gonadal structures on each side of a bilateral indirect inguinal hernia.

Such findings are infrequent, according to the literature, and are reported here for the purpose of calling attention to the complications that may arise in so common a condition as inguinal hernia.

BIBLIOGRAPHY

- ¹ Jopson, J. H. Hernia of the Uterus Through the Inguinal Canal. *ANNALS OF SURGERY*, 40, 98-116, 1904.
- ² Andrews, F. T. Hernia of the Uterus. *Tr. Am. Gynec. Soc.* 31, 407-426, 1906.

- ³ Makkas, M Hernia Uteri Inguinalis Bilateralis Deutsch Ztschr f Chir, 106, 401-406, 1910
- ⁴ McNealy, R W Strangulated Tubo-Ovarian Hernia in an Infant J A M A, 62, 772, 1914, *Idem* Sliding Hernia of Fallopian Tube Intnat Clin, 4, 30, 1920
- ⁵ Ludington, N A Case of Uterus and Both Ovaries in Indirect Inguinal Hernia Sac N Y Med Jour, 111, 986, 1920
- ⁶ Deutschman, D Complete Congenital Absence of Vagina, Associated with Bilateral Hernias of Uterus, Tubes and Ovaries N Y Med Jour, 118, 570-571, 1923
- ⁷ Sarnoff, J Hernia of Uterus and Tubes Through Inguinal Canal (Salpingohysterocoele) Case Report Am Jour Obstet and Gynec 15, 704-707, 1928
- ⁸ Hilarowicz, H Inguinal Hernia Containing Ovary, Tube and Horn of Uterus Zentralbl f Chir, 55, 2881-84, 1928
- ⁹ Reinberger, J R, and Simkins, C S Analysis of Human Ovotestis Associated with Congenitally Bisected Uterus Herniated into Inguinal Canals Am Jour Obstet and Gynec, 36, 275-281, 1938
- ¹⁰ Watson, Leigh F Hernia Anatomy, Etiology, Symptoms, Diagnosis, Differential Diagnosis, Prognosis, and the Operative and Injection Treatment Second Ed, Mosby, St Louis, 1938

PRODUCTION OF A THROMBOTIC BARRIER IN THE TREATMENT OF VARICOSE VEINS^{*}

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THIS PAPER IS concerned with the description of a simple, nonoperative method for limiting the chemical thrombophlebitis following retrograde injection of the internal saphenous vein during high ligation to the thigh portion of that vein

Retrograde injection of the internal saphenous vein during ligation was first practiced by Tavel¹⁰ in 1904. Moszcovitz,¹¹ in 1927, reemphasized its advantages. However, the level of ligation described by both these writers was considerably lower than that at which it is performed today. In 1934, Edwards,³ in an excellent anatomic study graphically illustrated how the point of ligation of the internal saphenous vein has gradually moved upward, so that today it is generally accepted that ligation of this vein should be done at the femoral junction with separate ligation of all available tributaries. In this country, Faxon,⁴ in 1934, was first to describe the advantages of retrograde injection. Since that time, this method of treatment of varicosities involving the internal or great saphenous vein, that is, high ligation at the femoral junction, with separate interruption of all tributaries entering into it, and the injection of a sclerosing solution distally, has come to be accepted as the most efficient mode of treatment in cases where there is evidence of incompetence of the valves of this vein, as demonstrated by a positive Trendelenberg test.

The Thigh Portion of the Internal Saphenous Vein—It is interesting to note that early in the injection treatment of varicose veins the failure to obliterate the thigh portion of the internal saphenous vein was recognized as a primary, if not the most important, cause of recurrence. DeTakats,² in 1930, and McPheeters,⁸ in 1931, stated that the existence of a column of blood in the unobliterated thigh portion exerts pressure upon the thrombosed varicosities in the leg and so contributes to their recurrence. McPheeters,⁹ in order to eliminate the patent thigh portion, recommended injection of the internal saphenous vein from ankle to thigh in one sitting.

It would seem that there are three main factors involved in the recurrence of varicosities that have been thrombosed by injection without previous ligation. The first is the fact that all thrombi have a physiologic tendency to recanalize unless the irritating agent has caused a very severe inflammatory reaction involving the entire vein wall. The second factor has recently been well illustrated by the work of Adams,¹ who showed that the pure gravity effect of a column of blood from the right auricle to a point of measurement in the mid-calf produces a pressure of 64 to 88 mm of mercury in the standing position in patients with varicose veins regardless

* Presented before the Chicago Surgical Society, May 1, 1942

of whether the valves are competent or not. He pointed out that the presence of functioning valves has no effect on this gravity pressure since the fact that this venous system is full of fluid (blood) fulfils the requirements of Pascal's law. The third factor is the effect of straining on this standing or gravity pressure. Adams found that straining caused the pressures mentioned above to be increased by from 12 to 136 mm of mercury resulting in a pressure of 224 mm in one of his cases, a figure far above the normal systolic arterial pressure. The increase in pressure produced by strain he has shown to be particularly high in individuals with incompetent saphenous valves. After high ligation the straining pressures were reduced by from 20 to 110 mm of mercury.

The work of Adams, thus, very well illustrates the value of ligation. However, it is evident that ligation alone, without a simultaneous obliteration of the thigh portion of the internal saphenous vein, would still leave a column of blood exerting a pure gravity pressure on the leg veins. Adams' work, thus, corroborates the rationale for retrograde injection since this procedure, when successful, insures the obliteration of the thigh portion of the internal saphenous vein.

Untoward Reactions Following Retrograde Injection—Retrograde injection of a sclerosing solution at the time of ligation is now quite generally accepted as the method of choice in the treatment of varicose veins involving the internal saphenous vein in cases where its valves are shown to be incompetent by means of the Trendelenberg test.^{5, 6, 7, 10, 12, 13, 14, 16} However, the writer has frequently witnessed very marked reactions following this procedure. In his experience this is particularly true in patients with extensive varicosities in whom the ensuing chemical thrombophlebitis and periphlebitis, involving as it does the whole internal saphenous tree, causes disability for a week or longer.

ILLUSTRATIVE CASE REPORT

Mrs. R. C., age 52, on examination, May 23, 1940, was found to have large varicosities involving the left internal saphenous vein. On the right side, there was moderate involvement of the external or small saphenous vein. The Trendelenberg test revealed a marked reflux phenomenon, and the Perthes test indicated normal patency of the deep veins. Point seventy-five cubic centimeters of sodium morrhuate was injected into one of the veins of the left leg, to make certain that the patient was not sensitized to this solution. Two days later, a high ligation of the left internal saphenous vein was performed, and four cubic centimeters of sodium morrhuate was injected distally. That evening, the patient complained of severe pain and discomfort. When seen the following morning, there was considerable redness, moderate induration, and marked tenderness all along the course of the saphenous vein from ankle to groin. The oral temperature was 104° F. This patient remained in bed for eight days. For the first six days, there was a low-grade fever ranging from 99° to 100.6° F. Codeine and hypnotics had to be administered to keep the patient in a degree of comfort.

It is obvious that this type of reaction tends to defeat the ambulatory nature of the injection treatment. Lowenberg⁷ has called attention to similar experiences. In 1937, he stated that in order to obviate the considerable

disability resulting from extensive swelling, pain, etc. he regularly ligated the saphenous vein at the knee prior to high ligation and retrograde injection, and thus limited the thrombophlebitic reaction to its thigh portion.

Retrograde injection of the internal saphenous vein during high ligation has been practiced in this clinic since 1936. The writer has always felt that the problem of eliminating varicosities of the internal saphenous vein was essentially a problem of sclerosing its thigh portion. About 80 per cent

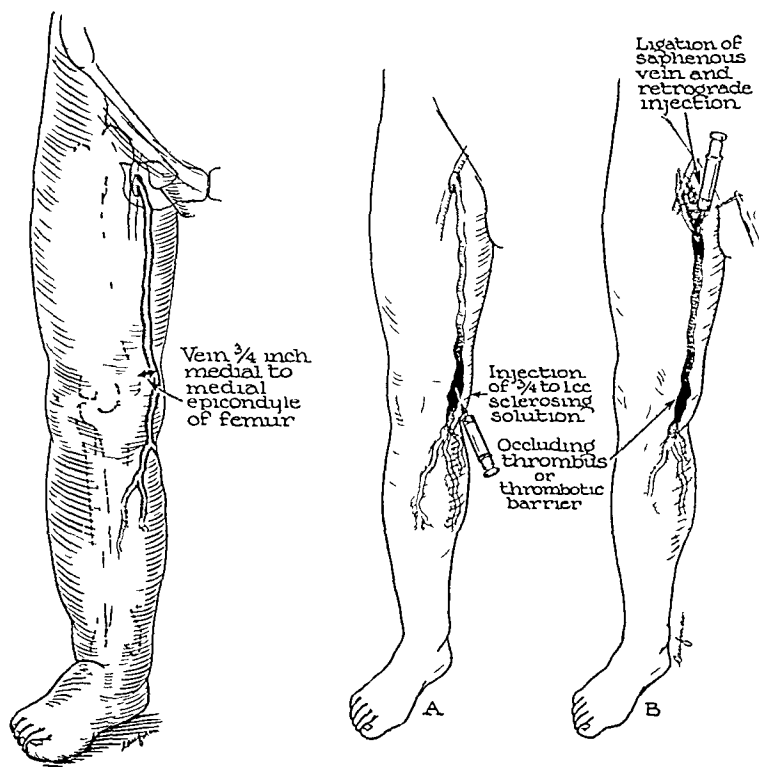


FIG 1—Drawing illustrating the relationship of the internal saphenous vein to the medial epicondyle of the femur

FIG 2—Drawings showing the proper location of the occluding thrombus or thrombotic barrier. The optimum location is slightly above an imaginary horizontal line bisecting the patella

of cases of varicosities occur in women. In them, the thigh portion of the internal saphenous, unlike the leg portion, is covered by a thick layer of fatty tissue, making palpation of this vein in the thigh, for purposes of injection, often quite difficult. This is particularly true after simple ligation. In the experience of the writer, severe reactions following retrograde injection, as illustrated by the case report, and described by Lowenberg, occur in one-half to two-thirds of cases with severe varicosities. In the past year, the following method has been used to limit the chemical thrombophlebitis to the thigh portion of the internal saphenous vein in all cases where high ligation with retrograde injection is planned.

METHOD OF PRODUCTION OF THROMBOTIC BARRIER

The internal saphenous vein at the level of the knee is palpated. At this point, the vein will be found about three-quarters of an inch medial to the

medial epicondyle of the tennu (Fig 1) Its palpation is facilitated by the fact that the layer of fat at this level is much thinner than on the thigh proper The vein is injected with 1 cc of sclerosing solution (sodium morrhuate) The patient is asked to return in three or four days If no thrombosis has occurred, the vein is reinjected with 1.5 to 2 cc of solution depending upon the caliber of the vessel Any palpable tributary in the region of the knee is similarly treated Ligation and retrograde injection

is performed when a firm thrombus has resulted This usually takes ten to 14 days In this way, an occluding thrombus, or thrombotic barrier, is created which prevents the sclerosing solution injected into the internal saphenous vein at operation from passing below the level of the knee (Fig 2)

The experience with 95 cases in whom the production of a thrombotic barrier preliminary to ligation was attempted has been as follows In 62 cases (65 per cent), firm thrombosis of the saphenous vein at the knee was obtained after the first injection In 14 cases (15 per cent), two injections were necessary, while in 12 instances (13 per cent), three or four injections were required In seven cases (7 per cent), no thrombosis was obtained after four injections and ligation with retrograde injection was performed in the usual manner

Method for Locating the Internal Saphenous Vein in the Fossa Ovalis—

Many suggestions have been made for locating the internal saphenous vein in the fossa ovalis Briefly, the most common procedures employed are the following Estimating the location of the vein by measuring one inch medial

to the femoral artery, which is located by its pulsation, palpating the transmitted impulse over the vein at or near the fossa ovalis following percussion of the vein in the region of the knee or lower thigh, using the pubic tubercle as a fixed point and measuring an average of 15 cm below and 4 cm lateral to it, in order to locate the fossa ovalis

For the past six years, the following method has been employed for locating the internal saphenous vein in the fossa ovalis preliminary to ligation

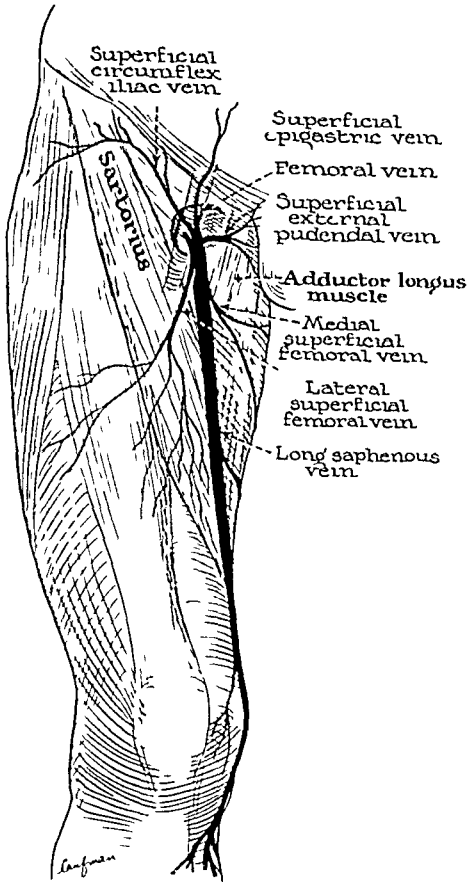


FIG 3—Drawing illustrating the relationship of the internal saphenous vein in the fossa ovalis to the easily palpable inserting portion of the adductor longus muscle The vein can be felt one half to one inch lateral to this landmark in the great majority of cases Note the relationships of the five main tributaries The upper two and occasionally even the superficial femoral veins may join the femoral instead of the internal saphenous vein

and for the performance of the Trendelenberg test. With the patient in the standing position, the examining fingers are placed over the thick, firm, adductor longus muscle at its tendinous insertion and are then moved one-half to one inch laterally, where the vein will be felt as a soft, yielding tube (Fig 3). It is easy to palpate the vein by the use of this method even in the most obese patient because of the fact that the layer of fat in this region, as over the knee, is relatively thin and also because the vein in the varicose state, is almost invariably dilated. The course of the vein is then traced on the skin with a dye.

Operative Technique—The operative procedure followed is essentially like that described by Faxon, and other writers. A short transverse incision, perpendicular to the dye mark, is made about one-half inch below the inguinal fold. The superficial fascia is then incised in a direction parallel with the skin incision. The vein is separated from the fatty and areolar tissues surrounding it and is then ligated high with No. 00 chromic catgut. This first ligature serves for traction downwards to aid the exposure of the two uppermost tributaries—the superficial epigastric and superficial circumflex iliac veins. These, if tributaries of the internal saphenous instead of the femoral vein, as they sometimes are, are separately ligated and severed. Another ligature is then placed on the saphenous vein above their point of junction. The superficial external pudendal vein is similarly treated. The lateral and medial superficial femoral veins, if present, are not ligated since that would prevent the sclerosing solution from entering them. Three to four cubic centimeters of sodium morrhuate are then injected into the saphenous vein distally. A No. 16-gauge needle, previously bent to an angle of 120° , to facilitate entrance into the vein, is used for this purpose. The vein is then ligated again about one inch below the point of injection and the segment of vein between the highest proximal and the distal ligature is excised.

Within 24 to 48 hours, the thigh portion of the internal saphenous vein becomes thrombosed. Often, in over one-half of the cases, the ensuing reaction is accompanied by considerable periphlebitis. However, none of these patients have been incapacitated for longer than a day. The injection of the patent leg varicosities is begun two weeks after ligation and is done at weekly intervals.

COMMENT—The comfort and the ability of these patients to engage in their usual pursuits has been in direct contrast to the discomfort and disability suffered by most patients who have been subjected to ligation and retrograde injection without the creation of a barrier at the knee. Possibly, the reason for the absence of disabling symptoms is to be explained by two factors. First, the limitation of the thrombophlebitic and periphlebitic process to a smaller surface, and second, the absence of inflammation in lower region of the knee and leg, resulting in painless locomotion.

SUMMARY

1 The combined ligation-retrograde injection treatment of varicose veins often causes considerable disability and discomfort in patients with marked involvement of the internal saphenous vein

2 A method is described whereby a thrombotic barrier, or occluding thrombus, is created in the internal saphenous vein in the region of the knee for the purpose of limiting the thrombophlebitic process to this level. This results in practically no disability to the patient. An experience with 60 patients is described.

3 A simple method for locating the internal saphenous vein in the fossa ovalis, preliminary to ligation or to performance of the Trendelenberg test, is described.

REFERENCES

- ¹ Adams, J. C. Etiological Factors in Varicose Veins of Lower Extremities. *Surg Gynec and Obst*, **69**, 717, 1939.
- DeTakats, Geza and Qunt, Harold. Injection Treatment of Varicose Veins. *Surg, Gynec, and Obst*, **50**, 545, 1930.
- ³ Edwards, E. A. Treatment of Varicose Veins, Anatomical Factors of Ligation of Great Saphenous Vein. *Surg, Gynec, and Obst*, **59**, 916, 1934.
- ⁴ Faxon, H. H. Treatment of Varicosities. Preliminary High Ligation of Internal Saphenous Vein with Injection of Sclerosing Solutions. *Arch Surg*, **29**, 794, 1934.
- Johnson, G. S. Recent Advances in Treatment of Varicose Veins. *Surgery*, **2**, 943, 1937.
- ⁶ Johnston, C. H. Combined Ligation and Injection Treatment of Varicose Great Saphenous Vein. *J A M A*, **109**, 1359, 1937.
- ⁷ Lowenberg, E. L. Varicose Veins Treated by Combined Ligation and Injection. *Surgery*, **2**, 903, 1937.
- ⁸ McPheeters, H. O., Merkert, C. E., and Lundblad, R. A. Causes of Failure in Injection Treatment of Varicose Veins. *J A M A*, **96**, 1114, 1931.
- ⁹ McPheeters, H. O., Merkert, C. E., and Lundblad, R. A. Mechanics of Reverse Flow in Varicose Veins as Proved by Blood-Pressure Readings. Its Clinical Applications to Injection Treatment. *Surg Gynec and Obst*, **55**, 298, 1932.
- ¹⁰ McPheeters, H. O. Present Status of Management of Varicose Veins. Collective Review. *Internat Abst Surg*, in *Surg, Gynec, and Obst*, **67**, 494, 1938.
- ¹¹ Moszcowitz, L. Behandlung der Kropfveine mit Zuckerinjektionen, kombiniert mit Venenligatur. *Zentralbl f Chir*, **54**, 1732, 1927.
- ¹² Ochsenr, Alton, and Mahorner, Howard. *Varicose Veins*. St. Louis, The C. V. Mosby Company, 1939.
- ¹³ Sears, J. B., and Cohen, S. S. Treatment of Varicose Veins by High Division and Retrograde Injection. Review of 125 Late End-results. *Surg, Gynec, and Obst*, **70**, 842, 1940.
- ¹⁴ Stalker, L. K., and Heverdale, W. W. Technique of Combined Division, Ligation, and Injection of Incompetent Great Saphenous Vein. *Surg, Gynec, and Obst*, **70**, 1094, 1940.
- ¹⁵ Tavel, E. Behandlung der Varizen durch die Ligatur und die kuenstliche Thrombose. *Cor Bl f Schweiz Aerte*, **34**, 617, 1904.
- ¹⁶ Zimmerman, L. M. Modern Management of Varicose Veins. *Illinois Med Jour*, **71**, 444, 1937.

HEMISECTION OF THE MANDIBLE FOR RECURRENT ADAMANTINOMA

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SINCE there have been a number of recent excellent reviews of adamantinoma, there is little indication for repetition. Hence, it is not our purpose to approach the subject from such a standpoint but merely to report two cases which were treated by hemisection of the mandible. Both cases had been treated less radically, on one or several occasions, with subsequent recurrences. It is of interest that the mutilation is less than might be anticipated even without dental prosthesis, and the result from a functional standpoint is gratifying.

Case 1—N. E., colored, female, age 29, was admitted to the Lakeside Hospital, June 27, 1934, complaining of swelling of the left side of the lower jaw, which had had its onset shortly after the extraction of a tooth some two years previously. Growth during the preceding nine months had been exceedingly rapid. During recent months the patient had had difficulty in separating the teeth more than one-half centimeter. The tumor mass was of the dimensions indicated in the photographs (PLATE I a and b) and in general was quite firm, although just below the zygoma it had a less firm character. The patient had a rather marked secondary anemia which could not be accounted for. On three different occasions partial resections and curettements had been carried out with ensuing recurrences.

Operation—October 31, 1935. Without preliminary ligation of the external carotid being carried out, a hemisection of the mandible was performed under intranasal catheter anesthesia. The mandible was divided through the symphysis and disarticulated at the temporomandibular joint. The mouth was opened into and an area of mucosa was removed with the jaw where it was intimately attached to the tumor. Considerable respiratory difficulty developed when the incision was extended posteriorly to the pharyngeal group of muscles, however, this was entirely corrected by the insertion of an airway. Closed intratracheal anesthesia might be useful, however, with reasonable care the above type of anesthesia proved quite satisfactory. The mucosa and submucosa were closed and a drain was inserted in the subcutaneous tissues at the posterior portion of the incision. The wound healed without a fistula in about five weeks. *Histologic Report* Adamantinoma.

One week postoperatively the teeth were wired to avoid deformity; the wire was removed after five weeks (Case 2 was not wired). The subsequent course was satisfactory and there was no evidence of recurrence of the lesion in the mandible. However, about six months later an obviously cystic swelling was noted in the left temporal fossa which gradually increased in size (dotted circle in PLATE I b). It was definitely in the temporal muscle and it was thought it represented an extension from the coronoid process or actual retraction of neoplastic tissues with the temporal insertion at the time of the resection of the mandible. On May 1, 1936, the left temporal fossa was exposed through an incision above the hair line, the zygoma was resected its full length for exposure and the cystic lesion was entirely removed. The premise previously suggested as to its origin was consistent with the findings. Examination in March, 1942, shows there to be a local recurrence in the temporal fossa but none in the region of the mandible.

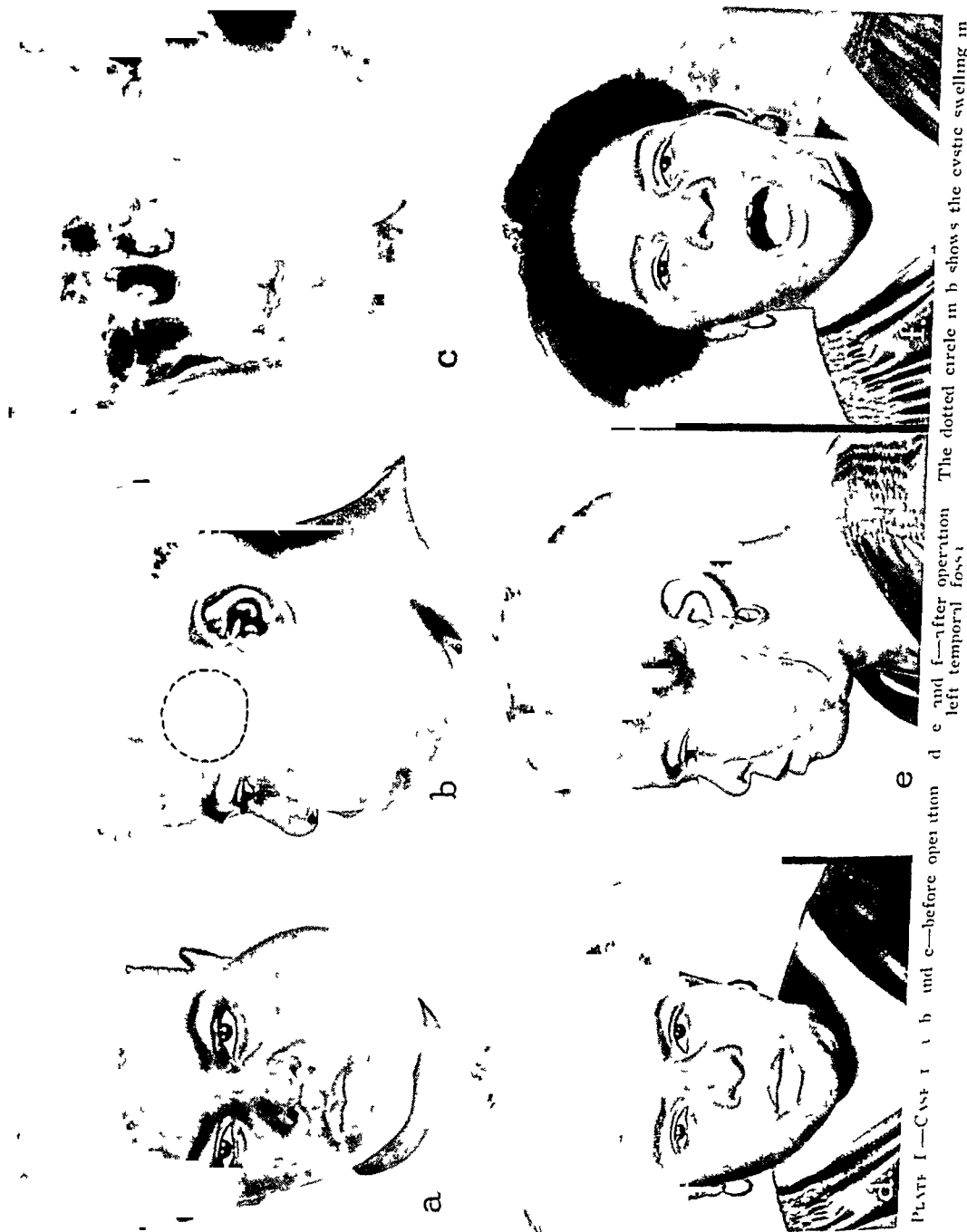




FIGURE II — (a) — before operation, (b) — before operation, (c) — before operation, (d) — after operation, (e) — after operation, (f) — after operation

Case 2—L J, colored, female, age 30, was admitted to Lakeside Hospital, September 30, 1932, complaining of swelling of the left side of the jaw which she had first noted some 12 years previously following the extraction of teeth. Increase in size had been gradual and not painful. The patient recently had noted cystic projection within the mouth. Examination revealed a swelling of the dimensions indicated in the photograph (PLATE II a and b), this swelling only slightly impaired the ability to open the mouth. To palpation exteriorly it was neither bony hard nor definitely cystic, however, there were several projections into the mouth which were definitely cystic. On October 4, 1932, partial resection and curettage were carried out. *Histologic Report* Dentigerous cyst (follicular).

The subsequent course was satisfactory for several years, however, cystic areas reappeared in the mouth, and roentgenograms revealed involvement of the mandible up to the temporomandibular joint. On January 29, 1937, hemisection of the mandible was carried out as described in the preceding case, although in this instance the resection was between the canine and lateral incisors. Examination of the resected specimen revealed the expansile effect of the lesion which was further manifested by the upward migration of the coronoid process (Fig 1). There might also have been a degree of

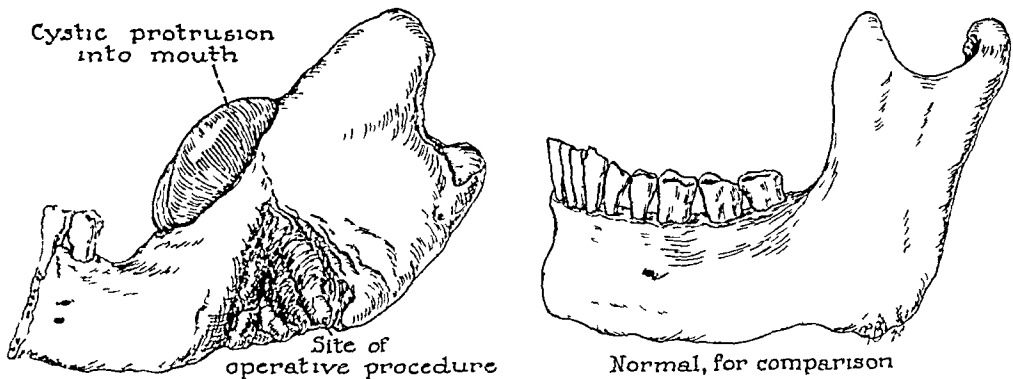


FIG 1—Case 2 Resected half of mandible

rotation as a result of the previous local resection of the mandible which might explain the apparent migration of the coronoid process upward. However, in other instances of expansile lesions we have noted apparent upward migration of the coronoid. *Histologic Report* Cystic adamantinoma.

The change in the pathologic diagnosis cannot be considered too significant in view of the similarity, microscopically, of the original lesion and the more cystic types of adamantinoma. The subsequent clinical course was satisfactory and there have been no recurrences to date.

While dental prosthesis might improve the cosmetic result, it was not employed in either of these cases. However, since the deformity is manifest by a flattening extending up to the level of the zygoma, this could not be entirely corrected by any form of dental appliance. The occlusion of the teeth of the remaining portion of the mandible is satisfactory and from a functional standpoint the patients can masticate quite well. The excellent muscle power may be demonstrated by noting the difficulty associated with the withdrawal of a tongue blade inserted between the teeth. Except for the loss of masticating surface there has apparently been little impairment of masticating efficiency of the remaining jaw. At no time have the patients complained of pain in the remaining temporomandibular joint as might be anticipated because of abnormal distribution of stress and strain. While from

the cosmetic standpoint a dental prosthetic appliance might be indicated, it is believed that from a functional standpoint it might place too much strain on the remaining temporomandibular joint, unless a fulcrum were established in the upper jaw on the resected side

In the first instance resection was, of necessity, carried out in the midline, and if any deviation of the chin occurs it is away from the side of resection. In the second case it was practical to resect between the incisors and canine teeth, and it will be noted that there is slight deviation toward the side of resection. Although the teeth were not wired postoperatively in the second case, we are inclined to believe that the discrepancy in deviation is due to muscle pull, *i e*, the nature of the muscle attachments remaining (largely the preservation of the origin of anterior belly of the left digastric). This may well explain the observed tendency to more marked deviations in unilateral resections of much less magnitude than hemisection.

Our limited experience would lead us to agree that the lesion should be widely excised, and if it is of any extent that hemisection should be given consideration. The mutilation incident to hemisection may be less than anticipated and from the functional standpoint largely represents a diminution of masticating surface. Kimm and Baranoff⁵ report a series of 26 cases of adamantinoma, in 13 of which they carried out hemisection of the mandible.

REFERENCES

- ¹ Bump, W. S. Adamantine Epithelioma. *Surg, Gynec, and Obstet*, **44**, 173, 1927.
- ² Carter, B. N. Adamantinoma of the Lower Jaw. *ANNALS OF SURGERY*, **94**, 1-6, July 1931.
- ³ Ivy, R. H., and Curtis, L. Adamantinoma of the Jaw. *ANNALS OF SURGERY*, **105**, 125-134, 1937.
- ⁴ Ivy, R. H., and Curtis, L. Hemorrhagic or Traumatic Cysts of Mandible. *Surg, Gynec, and Obstet*, **65**, 640-643, November, 1937.
- ⁵ Kimm, H. T., and Baranoff, A. F. Adamantinoma, Clinical Study of 26 Cases in Chinese. *Chinese Med Jour*, **53**, 1-22, January, 1938.
- ⁶ Simmons, C. C. Adamantinoma. *ANNALS OF SURGERY*, **88**, 693-704, 1928.

SO-CALLED DISLOCATION OF THE LOWER END OF THE ULNA

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"DISLOCATION of the lower end of the ulna" has been described as occurring after Colles fracture, in Madelung's deformity, in arthritis of the inferior radio-ulnar joint, as well as in a variety of other fundamentally dissimilar affections. Though the very diversity of the circumstances under which these so-called dislocations have been discovered should, in itself, have cast some doubt upon either the validity of the diagnosis or the unique nature of the underlying pathology, this has not been the case. Largely, it appears that the diagnosis depends upon the fact that dorsal prominence of the ulnar head, especially on pronation of the forearm, is a common and distinguishing feature of these different conditions. Yet when the roentgenograms of individual cases are studied closely, any conclusion justifying such a diagnosis seems to be open to very serious question. In one, there may be an abnormal disproportion in the length of the radius and ulna. In another, there may be a diastasis at the inferior radio-ulnar joint, without any change in the relative lengths of the bones. In a third, the most striking feature of the roentgenogram may be an axial malalignment of one or both of the bones, while in still another no bony abnormality whatsoever may be present.

The observations of these varied roentgenographic appearances becomes more significant when the effort is made to understand just what is meant by "dislocation of the inferior end of the ulna." If the term is employed in its usual connotation, it should imply a displacement of the inferior end of the ulna in relation to a more proximally located joint surface. Manifestly, this cannot be intended, since it does include the conditions under discussion. But even if its meaning were extended, so as to embrace displacements in reference to more peripherally located surfaces, the term would still describe no clearly definable anatomic concept. Because of the continuity of the ulnar shaft and the solid inclusion of its upper end in the elbow joint, dislocation of the lower end cannot occur, except as the result of fracture of the shaft. In fact, it seems there is no such condition as "dislocation of the lower end of the ulna." The term is a misnomer and is misleading, because it is not the ulna which dislocates in relation to the radio-carpal mass, but, on the contrary the latter which becomes displaced in respect to the stationary ulnar head.

Since, as will be seen, prominence of the lower end of the ulna is typical of a number of different affections, a more accurate designation, based upon their common symptomatology, appears to be desirable. In general, the whole group is characterized by weakness of the wrist, pain or tenderness on pressure, a clicking sensation on rotation of the forearm, and an abnormal prominence of the ulnar head. By analogy with the terminology used in

describing many injuries to the knee as "internal derangements," it seems reasonable to suggest a similar designation, "derangement of the wrist" for the disabilities here reviewed. This difference in terminology is of more than academic significance, because of the therapeutic consequences which each of the two concepts entails. The one leads to a search for and a

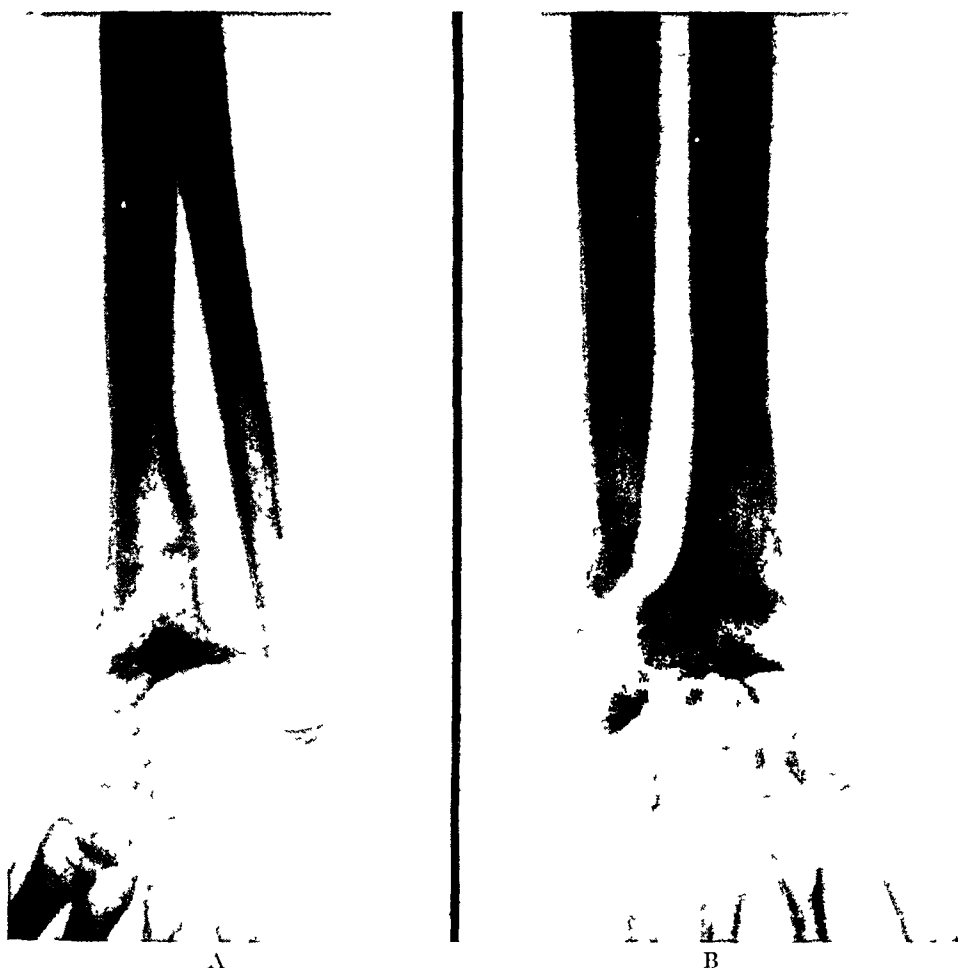


FIG. 1.—Case 1. (A) The site of the earlier osteotomy of the radius is to be seen. The lateral deviation of the hand persists due to abnormal projection of the ulna head below the level of the shortened radius. Note divergence of the forearm bones. (B) Following subperiosteal resection the lower end of the ulna has regenerated. The head is smaller and there is medial deviation of the ulna. Because of this the axial parallelism of the forearm bones has been restored even though the difference in length has not been corrected.

correction of the underlying pathology. The other leads quite naturally to the simple expedient of resection of the projecting end of the ulna.² In one case in which this method was applied a very interesting observation was made.

Case 1—T. S., age nine, was brought to the hospital in November, 1932, because of a painless swelling of the left wrist. The mother stated that the child's wrist had been "twisted" some two months before. Examination disclosed prominence of the left ulnar styloid. The hand was held in volar and radial deviation. There was no pain or tenderness. No limitation of motion was observed in the hand or fingers. Measured from the tip of the olecranon to the radial styloid, the left forearm was about one and one-quarter inches shorter than the right. Roentgenograms showed a separation of the bones at the wrist. The radius was short. The distal radial epiphysis was wide, mushroomed and sclerotic. The plane of the articular surface inclined acutely forward and medially.

In the face of the marked bony deformity, it was apparent that the recent history of trauma was merely coincidental and not of etiologic significance. In fact, the patient was considered as suffering from a Madelung's deformity, and a manipulative correction of the deformity was unsuccessfully attempted. In December, 1936, because of the progressive radial deviation of the hand, osteotomy of the radius above the epiphyseal line was undertaken. Despite this, radial deviation of the hand persisted. Roentgenograms taken one year later, in December, 1937, (Fig 1 A) disclosed a marked disproportion in the relative length of the forearm bones. The ulna projected not only below the level of the radial styloid but well beyond the proximal row of carpal bones, and even with the hand in radial deviation impinged against the carpal cuneiform. In October, 1938, a subperiosteal resection of the lower end of the ulna was performed and the forearm was immobilized in plaster for a period of eight weeks. Thereafter, physiotherapy was instituted. The patient has noted complete return of power and has no limitation of motion. She notes occasional pain on change of weather. Examination discloses but slight prominence of the ulnar head on pronation. The wrist is wider than on the opposite side. Roentgenograms (Fig 1 B), taken in December, 1939, disclosed the explanation of these phenomena. The lower end of the ulna has regenerated. Though its level with relation to the carpus has been changed but slightly, the ulnar head is definitely smaller and has clearly been deformed by medial pressure of the carpus. The fact that radial deviation of the hand disappeared after medial displacement of the ulna occurred seems to indicate clearly that it was the carpus and not the ulna which was "dislocated."

Though resection of the lower end of the ulna may indeed effectively eliminate the distressing prominence of its lower end, the possibility of injury to the ulnar collateral ligament with resultant disability is a danger to which Darrach has himself called attention.

From the functional point of view, the wrist is a compound joint, composed of the radiocarpal, the intercarpal, the meniscocarpal, and the radio-ulnar joints. In this complicated apparatus the head of the ulna forms a truly pivotal point. It is the point in relation to which the normal position of the other bony landmarks are determined and about which all of the motions of the wrist must be conceived of as occurring. It is the point to which are attached the ligamentous structures which fix the radiocarpal mass and thus insure free and forceful wrist motion. These ligaments comprise, roughly, three separate groups which diverge fan-like from their ulnar origin. The first, the triangular fibrocartilage, is attached to the inferior surface of the ulnar head and serves to unite the ulna with the sigmoid notch at the lower end of the radius. The second, the ulnar collateral ligament arises from the styloid tip, is firmly united to the base of the triangular fibrocartilage, and is inserted by two fasciculi into the cuneiform and pisiform bones. The third includes the anterior and posterior inferior radio-ulnar ligaments which arise from the lateral aspect of the ulnar head and bind it firmly into the ulnar notch on the radius. Loss of the integrity of either of these results in decreased fixation of the radiocarpal mass, with resulting prominence of the lower end of the ulna, and constitutes an indication for repair or reconstruction of the damaged ligaments, rather than ablation of the keystone upon which the functional integrity of the remaining structures depends.

The ulnar collateral ligament is probably the most important of these ligaments in stabilizing the wrist joint. Though the literature seems to indicate that injury to the triangular fibrocartilage is the primary cause of the weakness of the wrist joint⁹ it seems much more likely that this is frequently only coincidental to the more serious detachment of the ulnar collateral ligament.

The following case seen shortly after the reports of Mitchell⁸ and Gibson¹ is of interest in this connection.

Case 2—J. J., age 17, was first seen in June 1926, complaining of weakness and pain in the left wrist. The pain began on the ulnar side of the left wrist and radiated up into the forearm and down into the fingers. It was made worse by typewriting, so that the patient was forced to stop his work. He occasionally complained of weakness in the fingers and a clicking sensation on rotation of the forearm.

On questioning, it appeared that during a baseball game in 1924, the patient had suffered an injury while sliding into base with the outstretched left hand in full pronation. He complained of immediate pain and a marked prominence over the lower end of the left ulna. One of his friends "pulled his wrist out" and the patient felt something snap into place. Shortly thereafter he was seen by a physician, who stated that the patient had suffered a fracture of the wrist. Treatment consisted of splinting for a period of two months, after which the patient returned to work. In the early part of 1926 the patient began to notice pain and a gradual prominence of the lower end of the ulna.

Examination disclosed what appeared to be a marked hypermobility of the ulna both forward and backward. On pronation, the ulna became definitely prominent on the dorsum of the wrist. As the hand was pronated and supinated a soft click could be felt and heard over the head of the ulna. There was no limitation in motion of the wrist. On the right side a radial deviation of the hand to 20° was possible. On the left side, this was possible to 35°. When the hand was examined in this position, there was a distinct depression to be felt just beneath the ulnar styloid. The whole hand could be abnormally displaced forward and to the radial side. There were no weakness or sensory disturbances in the hand or fingers. Clinically there appeared to be no change in the position of the bony landmarks.

The roentgenograms were reported by Dr. A. B. Ferguson as follows: "The styloid process of the ulna is separated from the shaft at its base. This condition is believed to be a developmental abnormality. No other variation from the normal is noted at this examination." However, it is to be noted that there is a definite anterior dislocation of the carpus and that the head of the ulna articulates with the radius at its normal level (Fig. 2 A and B).

Despite this it was felt that the patient had probably suffered a fracture of the ulnar styloid, with rupture of the ulnar collateral ligament and the attachment of the triangular fibrocartilage. Since the fracture of the styloid did not seem to be the cause of the symptoms, it appeared likely that the disability was to be attributed to the soft tissue injury and exploration of these structures was undertaken.

Operation—July, 1936. Through a longitudinal ulnar incision, the course of the ulnar collateral ligament was exposed. The ligament was found attached to the tip of the styloid process. The triangular fibrocartilage, still partly attached to the ulnar styloid, was completely torn away from the inferior surface of the ulnar head. The relationship of the head to the radius appeared undisturbed. An effort was made to suture the fibrocartilage to the edge of the ulna and a heavy chromic suture was taken through the styloid process to unite it and the attached ulnar ligament to the tip of the ulna. The wound was closed in the usual manner and a plaster of paris bandage

was applied. At the end of four weeks this was removed and gentle, active motion was begun.

The patient made an uneventful recovery and shortly after reported the return of normal use of the wrist.

Somewhat similar experiences have been reported in regard to isolated injuries to the inferior radio-ulnar ligaments. Disabilities due to disturb-



FIG 2—Case 2 (A) The bones are of relatively normal length. There is a slight diastasis of the radio-ulnar joint but the ulnar head articulates normally with the notch on the radius. There is no radial deviation of the hand. (B) Lateral view discloses the dorsal prominence of the ulnar head, "so called posterior dislocation of the ulna simulated by anterior displacement of the radiocarpal mass."

ances in these structures present essentially the same symptoms and signs as are characteristic of the whole group of wrist joint derangements. In addition, however, the roentgenograms disclose a diastasis at the inferior radio-ulnar joint, the bones being of normal length. This, of course, is the pathognomonic sign, and the one which indicates the necessity for repair or reconstruction of the involved ligaments.

In 1926, the writer⁶ devised a fascial loop operation designed to accomplish this purpose. The procedure seems to have met a definite indication, in the opinion of other surgeons. With but slight modification it is almost identical with the operations later described both by Eliason,³ and by Lowman.⁵ However, attention must be called to the important fact that this technic is indicated, when and only when, the luxation occurs without loss of the normal bony alignment. It is intended strictly for repair of the

ligamentous apparatus and can have no successful application unless the bony disproportion has been previously corrected. Indeed, the necessity for reestablishing normal bone relationships before undertaking any ligament reconstruction, formed the basis of the conversation to which Lowman referred in his report of 1930.

The bone disproportions which may be found in derangement of the wrist fall into three main groups. Each presents the general features of the larger class of wrist derangements and, in addition, at least one distinguishing sign, which justifies its special consideration. The first of these groups is characterized by a loss of parallelism, an angular deviation in the axis of one or the other of the two bones of the forearm. Most commonly the radius is the site of angulation such as is found in Madelung's deformity or in a malunited fracture. Occasionally, however, the deformity may be caused by disease or malunion in the ulna. As regards the inferior radio-ulnar joint, the effects from the involvement of either of these bones may be identical and the only difference will be in the point of application of the corrective forces. In this type of case, simple osteotomy, for correction of the malalignment, is usually, but not invariably, sufficient to overcome the disability, as Campbell,¹ and others have pointed out. In those cases in which additional repair of the ligaments is necessary, the osteotomy constitutes an essential preliminary step.

The second group is characterized primarily by a disproportion in the relative lengths of the two forearm bones. Normally, the ulnar notch on the radius is approximately at the same level as the ulnar head, while the radial styloid projects at least one-half inch beyond the ulnar styloid. As a consequence of the greater length of the radius, the lower end of the ulna is at some distance from the carpus, so that any interference with pronation and supination is avoided. However, when this arrangement is disturbed and the ulna projects beyond the level of the radius, the ulnar head impinges against the carpus, with resultant limitation of rotation and subsequent relaxation of the ligamentous fixation of the wrist. This may occur in other conditions (see Case 1), but it is typically an end-result of improperly reduced Colles fractures and seems to be the cause of the disability to which so much attention has recently been directed.

With the object of determining this point a number of cases of Colles fracture were examined. In those in which symptoms of weakness persisted it was found that a relative shortening of the radius was an almost invariable finding. Careful examination of the radiographs in such cases demonstrated that the ulnar head projected well down over the shadow cast by the carpal bones. The impression was gained that in rotation of the wrist, the carpal bones impinged against the projecting ulnar head and forcibly caused its dislocation. It seemed reasonable to believe that the cause of the so-called luxation lay primarily in the bone block and that elimination of the osseous disparity would lead to disappearance of the symptoms.

The opportunity for testing the validity of this conception was offered by several patients, who presented themselves for the treatment of post-fracture "ulnar dislocations." Though specifically admitted with the intention of performing a fascial graft reconstruction, roentgenographic study suggested the desirability of preliminary shortening of the ulna by a cuff resection.⁷ The following typical case proved that no ligamentous reconstruction operation was necessary.



FIG. 3—Case 3. (A) The hand is displaced radialward. The ulnar head projects below the level of the radial notch and clearly impinges on the carpal cuneiform. (B) Union has occurred after subperiosteal cuff resection through epiphyseal line with shortening of the ulna. The head articulates with the radial notch and no longer impinges against the carpus.

Case 3—T. H., age 16, appeared in the Out-Patient Department, in April, 1939, complaining of weakness in grasp and difficulty in rotating his left forearm. In January, 1926, while sleigh riding, the patient had suffered a fracture of the left wrist, but no attempt at reduction had been made. The patient noted no trouble with his wrist until several months ago, when he began to observe a decreasing power of grasp and prominence of the lower end of the ulna.

Examination disclosed a radial deviation of the hand. The lower end of the ulna was prominent and at a level below the normal in relation to the radial styloid. Extension at the wrist was normal. Flexion was limited at 55° . Supination was about three-fourths normal. On pronation of the hand, the prominence of the lower end of the ulna became markedly exaggerated. Both ulnae measured $9\frac{1}{4}$ in. The right radius measured $9\frac{1}{4}$ in., the left only $8\frac{3}{4}$ in.

Roentgenograms, taken May 8, 1939, (Fig. 3 A) showed "an old oblique fracture of the anterior aspect of the distal end of the left radius, just proximal to the epiphyseal

plate There is a slight separation of the distal end of the left radius, just proximal to the epiphyseal plate There is a slight separation of the distal epiphysis of the ulna and a separation of the distal radio-ulnar joint There is a definite disproportion in growth between the ulna and the radius with the ulna projecting below the radius The epiphyseal lines are not closed"

Operation—May 22 1939 Under general anesthesia, a two-inch incision was made over the lower end of the left ulna The bone above the epiphyseal line was exposed subperiosteally A block of bone, including the epiphyseal plate, measuring about three-

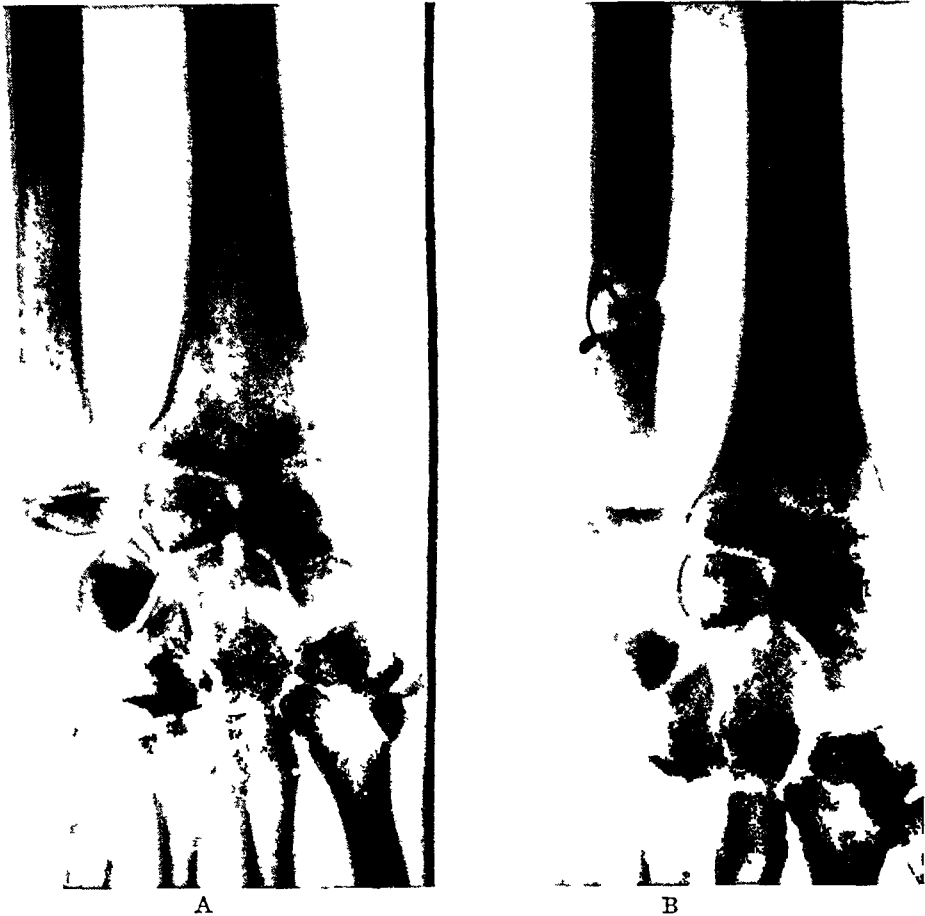


FIG 4—(A) Case 4, previously reported⁷ As a result of fracture, the articular plane of the radius is abnormally inclined medially and the ulnar head projects below its normal level (B) After subperiosteal cuff resection above the epiphyseal line the ulna has been shortened so that its head articulates with the radial notch Despite the abnormal medial angulation of the articular surface, normal function of the wrist was restored

quarters of an inch, was resected Holes were drilled in distal and proximal fragments, which were then drawn together, with chromic sutures The periosteum was reunited, and then the skin wound was closed A plaster of paris bandage was applied from the fingers to the midarm, with the elbow fixed at right angles and the forearm in mid-pronation

On June 22, 1939, the plaster encasement was removed Roentgenograms taken at this time (Fig 3 B) showed union of the fragments The longitudinal alignment was good, but there was a moderate rotation of the ulnar fragment The patient was given physiotherapy In October, 1939, it was noted that the correction was excellent There was no evidence of "so-called" dislocation of the distal end of the ulna and no weakness, despite the rotation of the distal ulnar fragment

Case 4—This case has been previously reported⁷ (Fig 4)

In Case 3, the cuff-resection was purposely planned so as to include the epiphyseal plate Except where it is intended to prevent further growth

of the ulna, it is better to perform the operation about one inch or one and one-half inches above the head of the ulna. This facilitates the fixation of the lower fragments and precludes the possibility of interference with radio-ulnar motion by excess callus formation, at the joint level. The plane of the resection may be at right angles to the shaft (Fig 4 A and B) or may be made oblique.

Experience in the treatment of Colles fracture has shown that the disproportion in the lengths of the forearm bones which is due to impaction and relative shortening of the radius is of the most serious consequence. The limitation of motion which is occasioned by improper alignment of the inferior radial surface is of comparatively slight importance. While every effort should be made to correct all deformities during the initial setting of the fracture, far too much attention is devoted to reposition of the articular surface and far too little to restoration of the relative length of the radius. Where this is overlooked "dislocation" of the ulna, pain, weakness, and limitation of rotation result from the impinging of the ulnar head against the carpal cuneiform.

In young children the disproportion in length between radius and ulna may be prevented or partly overcome by fusion of the lower ulnar epiphysis so as to arrest its growth. However, in adolescents near the age of normal epiphyseal closure, and in adults in whom the epiphyseal line has already been obliterated, the growth arrest operation is, of course, not applicable. In such instances simple shortening of the ulna to restore the anatomic proportion between the bones is sufficient to obviate the symptoms and usually precludes the necessity of any further operative reconstruction of radio-ulnar ligaments.

The third group is that in which the ulnar prominence is due either to arthritis at the radio-ulnar joint, or to disease of the ulnar head. In this event, of course, the hope of retaining the function of the radio-ulnar joint is illusory and resection offers the most expeditious form of therapy. Under certain circumstances, however, it may be desirable to preserve the ulnar head and its attached ligaments. In such cases, fusion at the radio-ulnar joint, with the subsequent formation of a pseudo-arthritis by cuff-resection of the ulna, just above the head, is suggested. This principle of treatment was employed with success in the following case.

Case 5—M. W., female, colored, age 28, entered the Out-Patient Department, December 31, 1934, complaining of a painful swelling of the right wrist of four days' duration. Gonococcal infection was denied. There was a history of influenza two weeks before the onset of symptoms, and it seemed reasonable to believe this was the origin of the infectious arthritis of her wrist. Nevertheless, in the course of routine investigation, the patient was found to be suffering from a bacteriologically established endocervicitis. A moulded plaster of paris cock-up splint was applied to the hand and forearm, with much relief to the patient.

In May, 1935, it was noted that ankylosis of the right wrist had occurred, with the hand in 15° of flexion. Rotation of the forearm was markedly limited. Supination was possible to only 15° beyond the neutral position. The lower end of the ulna projected

posteriorly and appeared to be subluxated. Roentgenograms showed absorption of the articular cartilage covering the carpal bones, the wrist, and the radio-ulnar joints (Fig 5 A). To correct the palmar flexion and the pronation deformity, open operation was decided upon.

Operation—December 19, 1935. Through a dorsal incision, the wrist joints and the lower end of the ulna were exposed. The ulnar head was dislocated posteriorly and the radio-ulnar joint was filled with connective tissue. The radiocarpal joint was the site of a destructive arthritis. The radio-ulnar joint was cleaned out and the dislocation of the ulnar head was overcome. The lower portion of the ulna was subperiosteally exposed and one and one-half inches of the bone above the head was

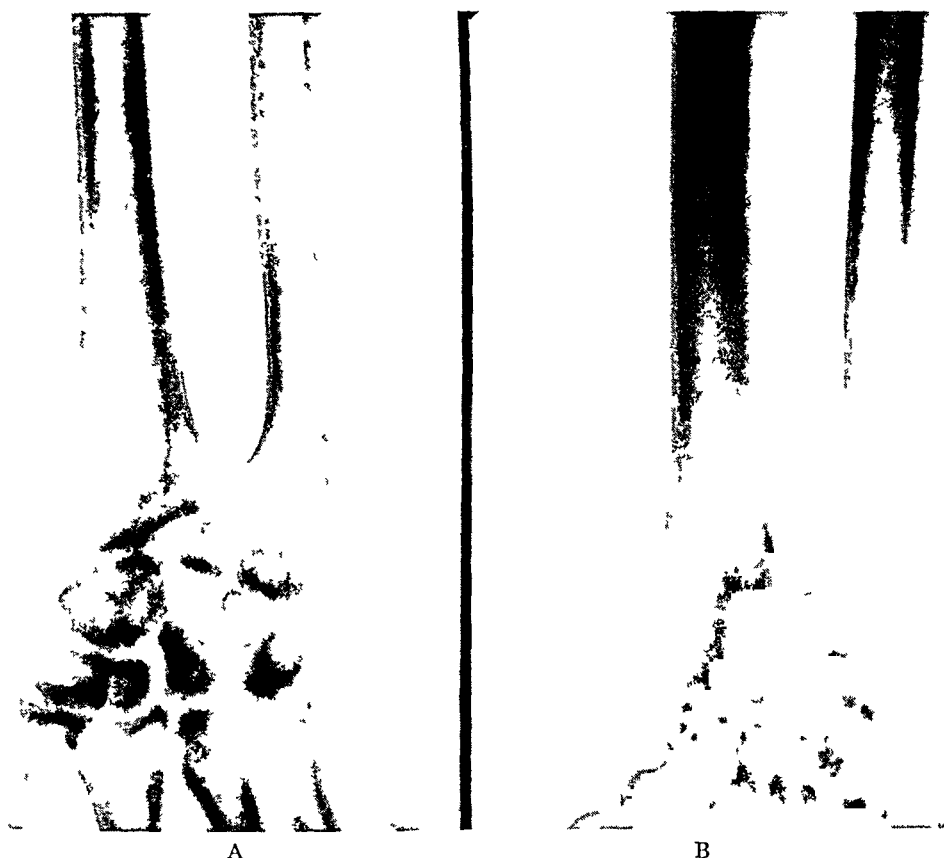


FIG 5—Case 5. (A) Arthritis of the wrist with dorsal prominence of the ulnar head. The carpus is elevated and impinges against the ulna. The relative length and axial parallelism of the bones is retained, with barely any radio-ulnar diastasis. (B) Postoperative. The radiocarpal and radio-ulnar joints have been fused. To restore the power of rotation a cuff resection of the ulna has been performed.

resected. The ends of the bone were covered with a muscle flap. The wrist joint was then opened and thoroughly curetted. The wrist was brought into dorsal extension and the position was maintained by sutures taken through the adjacent bone surfaces. The wound was closed without drainage, and a plaster of paris bandage was applied, with the forearm in supination and the wrist in 25° dorsal extension. The postoperative reaction was uneventful and the patient was discharged one week after operation.

The usual ambulatory treatment was carried on in the Out-Patient Department. As early as May, 1936, it was noted that the patient had solid fusion of the wrist, with return of excellent pronation and supination. The prominence of the ulnar head had completely disappeared. Roentgenograms, in December, 1936, revealed the fusion and the area of ulna resected (Fig 5 B). Examination, in April, 1939, disclosed the persistence of painless rotation. The only complaints were directed to pain and stiffness in the fingers, which were involved in the arthritic process.

CONCLUSIONS

So-called dislocation of the lower end of the ulna is a misnomer. Prominence of the ulnar head is a characteristic of a number of different conditions, which are more accurately to be designated as derangements of the wrist joint.

The head of the ulna may be considered as a fixed point about which the motions of the wrist joint occur. To it are attached the ligamentous structures which stabilize the wrist and which are necessary to its normal function.

Prominence of the ulnar head may be caused by

- 1 Injury to the triangular fibrocartilage
- 2 Injury to the ulnar collateral ligament
- 3 Rupture of the radio-ulnar ligaments
- 4 Axial deviation of either of the forearm bones
- 5 Disproportion in length of the forearm bones
- 6 Enlargement or disease of the ulnar head

Except for specific indications, the ulnar head should be spared and surgical attention should be directed toward repair or reconstruction of the ligamentous apparatus.

Repair of the soft tissues of the wrist can only be undertaken successfully if the bony relationships are normal, or have been previously restored to normal by appropriate types of osteotomy. For axial malalignment, simple linear osteotomy of the involved bone is sufficient. For disproportion in length, shortening of the ulna has proven extremely satisfactory.

REFERENCES

- ¹ Campbell, W. C. *Operative Orthopedics*. C. V. Mosby Co., St. Louis 1939, p. 1121.
- ² Darrach, Wm. *Jubilee Volume to Albin Lambotte*. Vromant and Co., Brussels 1936, p. 147.
- ³ *Idem*. Anterior Dislocation of Head of Ulna. *ANNALS OF SURGERY*, **56**, 802, 1912.
- ⁴ *Idem*. Habitual Forward Dislocation of the Head of the Ulna. *ANNALS OF SURGERY*, **57**, 928, 1913.
- ⁵ Eliason, E. L. An Operation for Recurrent Inferior Radio-Ulnar Dislocations, *ANNALS OF SURGERY*, **96**, 27, 1932.
- ⁶ Gibson, A. Dislocation of the Inferior Radio-Ulnar Joint. *Jour. Bone and Joint Surg.*, **7**, 180, 1925.
- ⁷ Lowman, C. L. The Use of Fascia Lata in Repair of Disability at the Wrist. *Jour. Bone and Joint Surg.*, **12**, 400, 1930.
- ⁸ Milch, H. New Operative Procedure for Dislocation of the Inferior End of the Ulna, *Amer. Jour. Surg.*, **1**, 141, 1926.
- ⁹ *Idem*. Die Fascienschlinge Operation, *Arch. f. klin. Chir.*, **151**, 176, 1928.
- ¹⁰ Milch, H. Cuff-resection of the Ulna for Malunited Colles Fracture, *Jour. Bone and Joint Surg.*, **23**, 311, 1941.
- ¹¹ Mitchell, A. Philip. Recurrent Anterior Dislocation of the Lower End of the Ulna. *Brit. Jour. Surg.*, **9**, 555, 1922.
- ¹² Taylor, W. G., and Parsons, C. L. Role of the Discus Articularis in Colles Fracture. *Jour. Bone and Joint Surg.*, **20**, 149, 1938.

THE TREATMENT OF FRACTURES OF THE OLECRANON BY LONGITUDINAL SCREW OR NAIL FIXATION

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THE INDICATION for operative reduction and internal fixation in fractures of the olecranon with separation of a sizable fragment is generally recognized. It is agreed, too, that open surgery with fixation of the fragments is required in comminuted fractures of the olecranon with displacement, and in fractures complicated by anterior displacement of both bones of the forearm. Until within the past few years the writer has been accustomed to use sutures of absorbable material as a means of fixation. A method that is proving to have certain advantages over such sutures is the fixation of the fragments by a longitudinal screw or nail. Not only is it possible to obtain reduction with greater accuracy and to ensure better retention of the fragments by this form of anchorage, but the period of disability is materially shortened. To the working man this decrease in the time element in recovery is of particular value.

Effective treatment of fractures of the olecranon depends upon two factors: (1) Accurate anatomic reposition of the fragments, and (2) sufficient fixation to permit immobilizing the elbow at a right angle. If the fragments are not replaced accurately, so that bony union takes place with perfect apposition, the power of complete extension may be lost. Moreover, as the fracture penetrates into the joint, any roughness or irregularity of the articular surface is not well tolerated, and arthritic changes will eventually develop. Following the reduction and fixation of the fragments, the elbow must be immobilized at a right angle, the position that is favorable both to healing and to the recovery of motion. The practice of splinting fractures of the olecranon in the position of extension, which still exists, is poor fracture therapy. In such cases, the convalescence is prolonged and the power of flexion is regained slowly. It may happen that, under this management, the fragments will separate upon the attempt to flex the elbow, or that complete flexion will never be recovered because of contracted tissues.

In the fulfillment of the requirements of efficient treatment of fractures of the olecranon, the use of a screw or nail for fixation is an advance over absorbable sutures. In a transverse or oblique fracture it is possible to obtain a hair-line apposition of the fragments and to fix them more tightly than when sutures are used. Particularly is this true when a screw is introduced, for, as it is threaded into position it tightly engages the fragments and closes the fracture-gap. In comminuted fractures, the main olecranon fragment can first be aligned with the ulnar shaft, and then the smaller fragments fall into position easily. In fractures of the olecranon associated

with anterior displacement of the forearm bones, in which accurate reduction and retention of the fragments are essential to the control of the reduced dislocation, the longitudinal fixation ensures perfect reposition.

Once this fixation material is in place, there need be no hesitation on the part of the surgeon in flexing the forearm to a right angle. In contrast, when absorbable sutures are used, there is the danger that they will not



FIG 1—Patient H S. (A) A transverse fracture of the olecranon with separation of the fragments. (B) Postoperative roentgenogram showing fixation of the fragment with a longitudinal screw.

FIG 2—Patient L D. (A) A comminuted fracture of the olecranon with displacement. (B) Roentgenogram taken five months after reduction, with longitudinal nail in place.

withstand the tension and that the fragments will separate as the forearm is flexed to the right-angle position for immobilization.

The great advantage of internal fixation by this means is the shortening of the convalescence. So accurate is the replacement of the fragments and so secure is their retention in position that motion may be started in from four to five days after the reduction. This is in contrast with the three or four weeks of immobilization that is necessary following fixation by other methods.

FRACTURE OF OLECRANON

The prompt healing affords relief from pain and soreness, so that the patient has the confidence to start motion early. Within a few weeks a good arc of motion is possible, whereas, in the case of sutured fragments the convalescent period extends over several months.

Operative Technique—The operation is best carried out in from three to five days after the injury, when the swelling will have subsided. A general anesthetic is administered and a tourniquet carefully applied.

A longitudinal incision is made, beginning one inch above the tip of the olecranon and extending downward to a point from one to one and one-half inches below the fracture-cavity. The incision is carried down to the periosteum, and the skin and subcutaneous tissues are retracted laterally to expose the fracture-cavity. The blood clots, tabs of torn periosteum, and minute detached spicules of bone are removed. Any fragment that retains sufficient attachment to ensure a blood supply is not disturbed. The ends

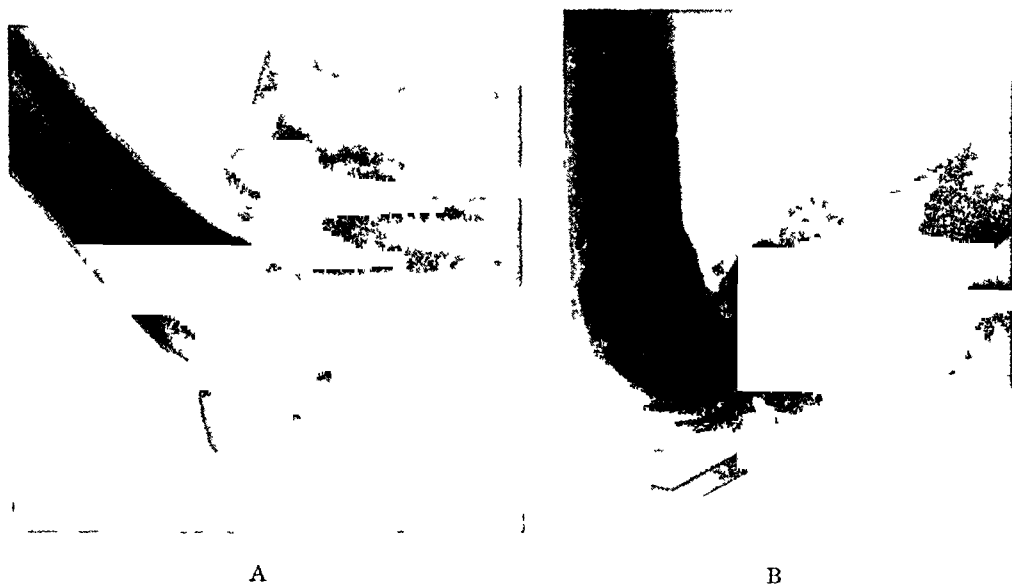


FIG. 3.—Patient R. J. (A) A fracture of the olecranon with anterior displacement of both forearm bones. (B) Postoperative roentgenogram showing fixation of the fragments with a longitudinal screw.

of the fragments are cleaned with pledgets of gauze. The forearm is extended, and the replacement of the fragments studied.

The forearm is then flexed about 15 degrees, and a short longitudinal incision is made in the triceps tendon above the tip of the olecranon. A small drill is inserted in the proximal fragment, at the tip of the olecranon, and forced through the fragment into the center of the fracture-cavity. The fragments are approximated and held in position by means of a tenaculum.

A screw of sufficient length to fix the fragment to the ulnar shaft is passed through the drill-hole and threaded into the ulna. If possible, it is well to so direct the screw that it engages the distal cortex of the ulna, thus providing for perfect fixation (Fig. 1 B). If a nail is used, it must be sufficiently long so that its tip engages the cortical bone beyond the bow of

the ulna (Fig 2 B) The lateral expansions of the triceps tendon are sutured with interrupted chromic catgut

In comminuted fractures, when the main fragments have been aligned, the smaller ones are easily fitted into place In the case of fractures of the olecranon associated with displacement of both bones of the forearm, the dislocation is first reduced and then internal fixation of the ulnar fragments is established

Following the closure of the wound, the elbow is immobilized at a right angle A posterior plaster shell may be applied and worn for a few days, but it is sufficient to use a tight bandage and carry the arm in a sling Exercises of the fingers and the shoulder are started on the second day the patient squeezing a rubber ball and abducting the arm hourly Through such exercises the tonicity of the muscles of the arm and forearm are preserved Gentle motion of the elbow, in flexion and extension, can usually be started on the fourth or fifth day after reduction At this time hot fomentations may be of help

The insertion of the screw or nail is a simple procedure and is easier, in fact, than the fixation of the fragments with sutures The screw or nail may be removed in about six months, but this is optional

CONCLUSIONS

Fixation of the fragments in olecranon fractures by a longitudinal screw or nail is a simple procedure that has certain advantages over the suture methods in general use By this method it is possible to obtain reduction with greater accuracy and to ensure better retention of the fragments Good functional recovery is established within the shortest possible time when this longitudinal fixation is used, a factor of importance to the active adult

THE REGENERATION OF JOINT TRANSPLANTS AND INTRACAPSULAR FRAGMENTS†

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IN DISCUSSING joint transplantation, it is important to distinguish between transplantation of entire joints and transplantation of one-half of a joint, furthermore, between autogenous and homologous transplantation. While transplantation of entire joints was soon given up as impractical, transplantation of one epiphysis or one-half of a joint, particularly if done autogenously, became a well-established procedure.

Tuffier³¹ (1901) was, supposedly, the first surgeon who performed a joint transplantation. In a fracture through the surgical neck of the humerus, he removed, temporarily, the head of the humerus and reimplanted it on the humeral shaft in a more favorable position. Tietze,³⁰ however, as far as can be ascertained, was the first who performed a genuine joint transplantation, he replaced the resected lower part of the radius with a phalanx of a great toe. The first experimental studies upon this subject were performed by Judet,¹⁶ in 1906. He studied the condition of the transplanted cartilage in rabbits and found the cartilage preserved in those cases in which he performed a reimplantation, *i e*, an autogenous transplantation of joint surfaces. In a second series of experiments he performed homologous transplantations of entire or half-joints, with or without capsule. The joints were transplanted beneath the skin of the other animal. In cases where the naked joint was transplanted, erosion of the graft by fibrous tissue occurred while the grafts transplanted with the capsule remained preserved. Impallomeni,¹⁵ Ducuing,¹⁰ and Voronoff³² had similar results. Dalla Vedova,⁹ however, observed a complete necrosis in those parts which were transplanted with the joint capsule, but large parts of those grafts transplanted without capsule remained alive.

It must be assumed that the most favorable conditions in joint transplantation will be those in which only one-half of the joint is replaced and the capsule of the host joint remains preserved. Gill¹² and Haas¹³ proved this in autogenous joint transplantations, and Rehn and Wakabayashi²⁴ in homologous transplantations. Gill autotransplanted the second long metatarsal bone in dogs from one paw into the opposite paw. After seven to eight months he found the articular surfaces normal and the joints had perfect function, the bone showed no evidence of necrosis. Haas, in a large series of experiments, studied the effect of transplantation of the epiphysis on bone and cartilage regeneration and the bone growth after reimplantation and autotransplantation of metacarpal and metatarsal bones in dogs. He concluded that the articular cartilage offers the greatest possibilities for successful transplantation of the various parts of a bone. The bone itself degenerates but later becomes regenerated from periosteum and endosteum, as Phemister,²² and others, have

† Read before the Philadelphia Orthopedic Club, January 9, 1941, at Philadelphia, Pa.

described it. The longitudinal growth stopped in every case because the epiphyseal line ceased to function. V. Tappeiner²⁹ came to a similar conclusion. Rehn and Wakabayashi—even in homologous transplantations—found the epiphyseal cartilage fully maintained in function and histologic structure after the transplantation.

After having studied the results of animal experimentation, it is interesting to compare them with joint transplantation in human beings. Lexer¹⁹ (1907) was the first who performed transplantations of entire joints together with menisci and crucial ligaments—however without capsule. This startling operation, mostly performed for replacement of ankylosed joints, was soon given up by its originator and replaced by simpler operations, namely, the joint plastic with interposition of fat tissue or fascia. Nevertheless, of the 23 cases in which Lexer performed such homologous transplantation, 12 cases resulted in the transplant healing and mobility remained for a number of years. Later, however, mobility decreased and became painful due to extensive arthritic changes. Two of those patients in whom entire knee joints had been transplanted—the transplant for one was taken from an executed criminal—could be followed for 14 and 16 years, respectively. Burkle-de la Camp⁶ later examined the specimens. The joint cleft was still preserved, but the cartilage was replaced by fibrous tissue, and there was extensive subarticular break-down of the subchondral cancellous bone. These consequences are apparently less serious in homologous half-joint transplantations where only one-half of the joint is replaced and the host capsule remains preserved (Lexer, Enderlen¹¹). They are, as shown by a number of authors, entirely absent in autogenous half-joint transplantations provided proper operative and post-operative precautions have been taken. Rovsing²⁵ (1910) successfully replaced the upper two-thirds of the humerus with the upper part of the fibula in the same patient. Klapp¹⁷ (1912), after a similar operation, followed his patient for seven and one-half years, there was hardly any limitation of function. Albee¹ reports several cases in which he resected the upper humerus for primary malignant tumors and grafted the upper part of the fibula into the defect. One patient was followed for nearly 17 years, there was good function and no evidence of recurrence. A number of similar cases have been published since, replacement of the upper half of the femur and the lower half of the radius by the upper half of the fibula, replacement of phalanges and metacarpal bones by bones of the foot (Behrend,³ Phemister,²² Portugolow,²³ Skillern,²⁷ etc.). But only rarely have specimens of these autogenous grafts been obtained for investigation of the regenerative processes. Conclusions gained from animal experiments are of doubtful value in those cases in which graft and host bone cannot be immobilized. More reliable results come from those experiments in which entire bones are transplanted (Gill, Haas).

I²⁰ reported recently about an experiment where I took out entire radius in dogs and returned them into their original places. Thus a transplantation of bones was combined with a transplantation of epiphyses. After injection

of the bone vessels with contrast material and visualization of the vessels roentgenographically, the specimens were examined microscopically. This examination showed that the bony parts and the medullary tissue died after transplantation. Later on, however, from two and one-half to four months postoperatively, the dead graft was transformed gradually into living bone tissue by osteoblasts which accompanied the periosteal vessels on their way through the haversian canals of the graft. Of the transplanted cartilages, the outer layer remained alive. Considerable parts of the deeper layers, however, were found dead primarily, but later stages showed these layers perfectly regenerated.

I should like to present a clinicobiologic study of the regeneration of joint transplants and of certain intra-capsular fragments, and shall attempt to parallel the two.

REGENERATION OF JOINT TRANSPLANTS CASE REPORTS

Case 1—L., age 43 (referred by Dr. Charles F. Mitchell), was admitted to the Geimantown Hospital in January, 1940, with a fracture-dislocation of the head of the right humerus (Fig. 1). After several unsuccessful attempts of closed reduction, an extension dressing was applied to the right arm, an open reduction had been planned but was postponed because of an extensive thrombophlebitis of the veins of the volar surface of the right arm. The operation was carried out March, 1940. The shoulder joint was opened by an incision that ran along the median border of the deltoid muscle and separated the clavicular insertion of this muscle (Henry, Thompson). The entire median half of the deltoid muscle was reflected laterally and backward, establishing an excellent exposure of the shoulder joint region. The next step was exposure of the head fragment. The head of the humerus could be felt beneath the pectoralis minor muscle. With considerable difficulty it was dissected free and temporarily removed. It was kept in normal salt solution for the time being. Now followed the subperiosteal exposure of the shaft of the humerus. After its stump was freed from cicatricial tissue, the head of the humerus was placed upon the shaft. A canal was drilled through shaft and head, the long biceps tendon was divided, threaded through it and sutured, according to Nicola. Thus the head of the humerus was not only fastened to the shaft of the humerus, but, also, the entire humerus kept in the glenoid. This fixation, however, was not sufficient. Therefore, I drilled two Kirschner wires through head and shaft in different directions, thus achieving an internal fixation of this fracture. The wound was closed in layers, the arm immobilized in right-angle abduction by a plaster encasement which included chest and the entire arm. The wound healed primarily, and the patient was discharged four weeks after the operation.

Five months after the operation the encasement was removed. Roentgenograms showed definite signs of union. Physiotherapy and motion exercise was started. About four weeks later the patient was readmitted. He stated that he had experienced a "fainting spell" (of alcoholic nature), and had fallen and broken the right arm again. This time the fracture was between the proximal and middle third of the shaft, while the former fracture remained firm. Judging from the size of the accompanying hematoma the fall must have been violent. The fragments were considerably displaced in angulation. This fracture was treated in extension with a Kirschner wire through the olecranon. It healed in good position (Fig. 1 b and c).

While the patient was in the hospital he developed a small superficial ulcer in his former scar. A prominence could be felt beneath this ulcer which was thought to be due to one of the wires working its way out of the replanted humeral head. For this reason operative removal was advised. I performed this operation in October, 1940.

(seven months after the first operation) The shoulder joint was exposed through the lower part of the former incision. No evidence of a true capsule could be detected. The head of the humerus was firmly united with the humerus. The head of the long biceps tendon was found incorporated in the bone. There was no evidence of slipping of either wire. Although their upper canals were visible it would have been difficult to remove them, and for this reason they were left in place. The prominence was due to callus formation, it was levered off. Two small pieces of the replanted head of the humerus were taken for microscopic examination. One consisted of cartilage together with a thin



FIG 1a—Fracture dislocation of head of right humerus
b Six months after temporary removal and reimplantation of head of humerus Frac-
ture of shaft of humerus after recent trauma
c One year and two months after the fracture dislocation

layer of underlying bone, the other one was taken from the same place but from deeper inside. Profuse oozing was encountered from both cut surfaces proving that the circulation of the head of the humerus had become reestablished. The patient was soon discharged to receive ambulatory physiotherapy. He has regained 50 per cent of the motility of his right shoulder in all directions, and is free from pain. He is employed as a truck driver and has recently lifted a trunk, weighing 155 pounds, from the truck to the scale and back again*. The patient was reexamined recently (two years after the operation). Roentgenologically the head of the humerus shows some "mushroom" deformity. Clinically and symptomatically there was no change.

* The histologic examination of the two specimens taken from the replanted head, seven months after the operation, revealed the following picture. A number of the lacunae of the bone were found empty, but in many other places the lacunae were filled with a well stained nucleus. The haversian canals contained blood vessels which were accompanied by osteoblasts. Rows of osteoblasts were also found along the trabeculae. On these trabeculae the difference between the living, *etc.*, the newly formed bone, and the dead bone was clearly visible and there was no evidence of osteoclastic bone destruction and absorption. The medullary spaces were filled partly with a vascular fibrous tissue, partly with normal medullary tissue, beneath the cartilage even myeloid tissue could be seen. The cartilage itself was found alive in its outer layer while the middle and deep layer showed empty lacunae in various regions.

COMMENT—An operation was performed for a fracture dislocation of the head of the humerus, during this operation the head of the humerus was temporarily removed and then replanted on the humerus shaft. Thus the head of the humerus could be compared with a half-joint transplant. It must be assumed that due to the complete interruption of circulation, the graft had died. But after its reimplantation vessels must have grown into the dead graft. The vessels were apparently derived from the shaft of the humerus and accompanied by intramedullary osteoblasts. These osteoblasts transformed the dead graft into living tissue by the so-called creeping substitution of the dead bone by new bone, as biopsy specimens, removed from the head of the humerus seven months after its reimplantation, revealed. The microscopic picture of these specimens were very similar to those which I²⁰ described in my former experimental work. The joint cartilage remained alive in its outer layer while sections of the deeper layers died. Thus, this autogenous joint transplant died in most of its parts, but was gradually regenerating from ingrowth of vessels and osteoblasts of the living bone, the ingrowth of these vessels was facilitated by a prolonged complete immobilization of the fragments.

This case is a typical example of an autogenous half-joint transplantation. Half-joint transplantation has become a well-established procedure. The autogenous transplantation within the same individual is preferred to the homologous transplantation due to better and quicker healing conditions. The disadvantage of the autogenous transplantation, however, is the limitation of the material to be transplanted, namely, the phalanges of the toes, the metatarsi and the fibula. So, for instance, the humeral part of the shoulder joint and the radial part of the wrist joint can successfully be replaced by the upper part of the fibula. Even the upper half of the femur has been successfully replaced by the fibula. If it comes to broader joint surfaces, however, particularly those which carry a socket, an autogenous transplantation cannot be performed. In those cases—if a half joint transplantation is considered at all, and a suitable donor available—the homologous transplantation is the only possibility. The following example, a short preliminary report which appeared in Brun's *Beitr. z. klin. Chir.*, 160, 30, 1934, might be recorded.

Case 2—Female, age 23, was admitted to the hospital, complaining of throbbing pains in the right knee joint of six months' duration. Examination revealed a tumor

within the lateral half of the upper fourth of the right tibia (Fig 2 a) The tumor had apparently broken through the cortex There was no evidence of metastases An amputation of the right lower extremity above the knee joint was planned in case the biopsy revealed a malignant tumor The amputation, however, was refused by the patient At the same time a male, age 70, was in the hospital who suffered from an arteriosclerotic gangrene of his right foot, with partial blocking of the popliteal artery, necessitating an amputation above the right knee joint

A compromise operation was now planned for the first patient Permission for such an operation was given Both patients had blood Group O The operation was carried

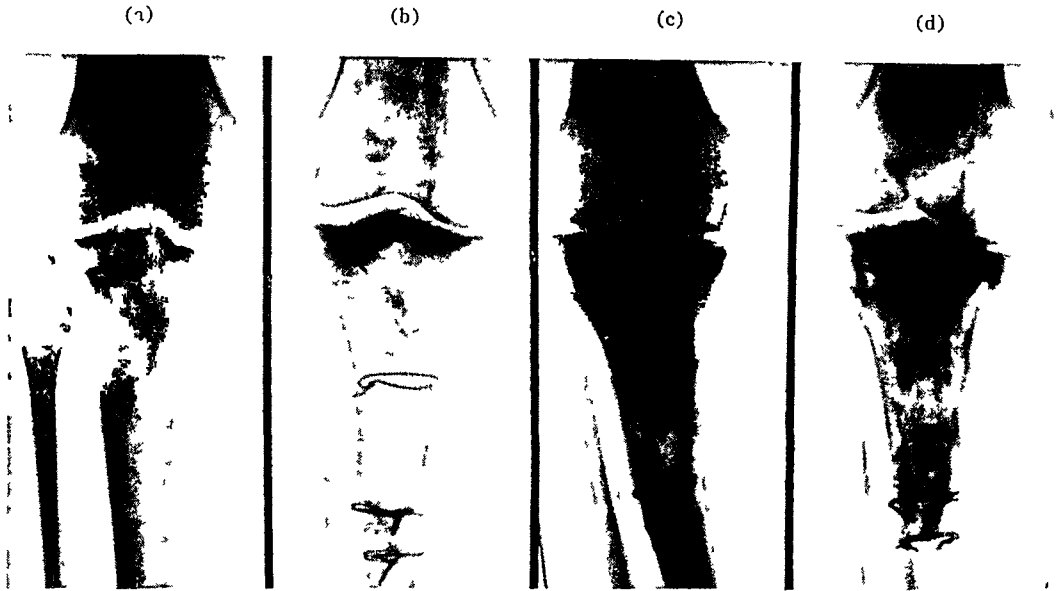


FIG 2(a) —Sarcoma of lateral condyle of right tibia with invasion of soft tissues in a 23 year old female

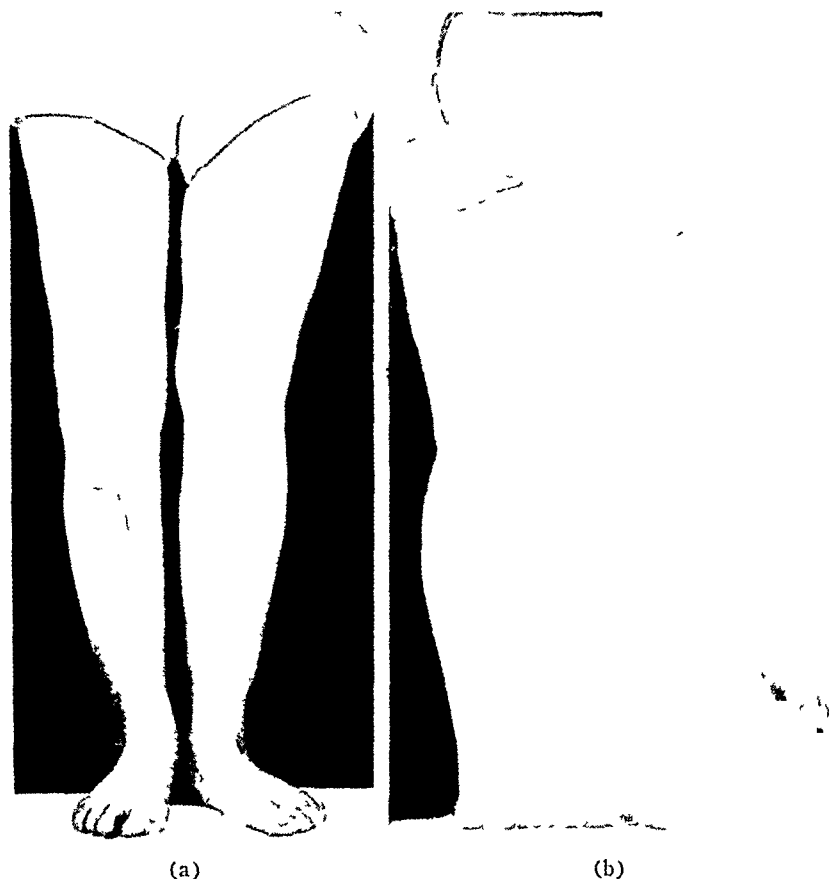
(b) Same patient eight months after resection of upper third of tibia and transplantation of the corresponding part of tibia from a 70 year old man Head of fibula and surrounding soft tissues had been removed at the same time

(c) Same patient two years after operation Fusion between tibia and graft

(d) Same patient five and one half years after operation, no evidence of recurrence, subarticular breakdown of median condyle of graft Roughening of articular surface

out in June, 1933 (operators, Lever-May) The biopsy confirmed the diagnosis of sarcoma From a Y-shaped incision in front of and below the right knee (Fig 3 a), the joint was opened after separation of the tibial tubercle, and lifting of it upward together with the skin flap and quadriceps tendon The tumor was now exposed It had penetrated into the soft tissues near the head of the fibula Then followed the separation of the crucial ligaments and of the median and lateral ligaments at their insertion at the tibia The head of the fibula with surrounding soft tissues, including one branch of the peroneal nerve and the upper third of the tibia, were now resected The tibial resection was staggering At the same time, in the same operating room, the corresponding part of the tibia of the male, age 70, had been resected in a similar way and was now transplanted into the girl's leg and fastened there with two wire loops The lateral and median ligaments were attached to the tibia transplant as well as possible The quadriceps tendon together with the tubercle of the tibia were fastened to the transplant with a wire suture The wound was closed in layers and the leg placed in a plaster encasement reaching from the toes to mid thigh Healing was uneventful Eight weeks after the operation the plaster encasement was replaced by a brace, in which the patient left the hospital Figure 2 b shows the roentgenographic findings eight months after the operation March, 1935, 21 months postoperative, the patient was allowed to discard the brace, she walked without the slightest limp or pain until six months later, when the patient complained of increasing pain and uneasiness in the right knee joint Roentgenograms

revealed a slight depression of the median knee joint surface, where most of the pain was concentrated (Fig 2 c) Since there was the possibility of a pathologic fracture at this site, the patient was operated upon again From the former incision the bone was exposed, the soft tissues were found to be in intimate connection with the graft, no fracture, no evidence of recurrence was found, just below the insertion of the quadriceps tendon a piece of the cortex was removed in order to inspect the inside of the graft Necrotic fat tissue and sand-like sequestria were emptied from the superficial spongy layers while deeper inside profuse bleeding was encountered The upper wire was now removed and the wound closed in layers After healing of the incision, the patient had



FIGS 3a and b—Same patient as in Figure 2 Two years after operation

to use the brace again for walking At the end of 1937 the patient was allowed to discard the brace again She could walk without any support A roentgenogram, five and one-half years after the operation, revealed no evidence of recurrence, and no further breakdown of the bony structure of the graft, but roughening of the joint surface (Fig 2 d) In spite of these changes and a moderate genu varum deformity, the patient walked without any pain or limp In January, 1939, she felt a dull pain in her epigastrium and noticed a gradually increasing swelling of both lower extremities and abdomen Before long she became jaundiced The family doctor advised against an operation The patient died, February 19, 1939, five and three-quarter years after the operation An autopsy was not performed

COMMENT—In a 23-year-old patient, the right upper third of the tibia was replaced by a corresponding part taken from a 70-year-old man Both patients had the same blood group It must be assumed that the bony parts of this graft died after transplantation—as in any other bone graft They were gradually regenerated, however, by creeping substitution of the dead bone by new bone While in autogenous grafts the regenerative process takes

a comparatively short time, in a homologous graft it takes years before the dead bone is substituted by a new bone. In the above case, the greater parts of the graft were still found dead after nearly two years post-operative. No wonder that some parts of the dead cancellous bone broke down upon weight-bearing. It must also be assumed that parts of the articular cartilage had become replaced by fibrocartilage or fibrous tissue, since, according to Phemister, articular cartilage dies if the regeneration of the bone beneath is delayed for longer than one year. Thus homologous half-joint transplantations should be considered only in exceptional cases. Autogenous half-joint transplantations are much more reliable, as clinical and experimental results demonstrate.

REGENERATION OF CERTAIN INTRACAPSULAR FRACTURES

The healing process of an intracapsular fracture of the neck of the femur and certain other intracapsular fractures have often been a matter of dispute, but more light has been thrown recently upon this subject since the regenerative processes in those types of fractures have been compared with those found in bone transplants, more correctly termed half-joint transplants (Axhausen,² Phemister²²). It is generally agreed that in an ordinary fracture the periosteum and endosteum are important healing factors from which most of the callus is derived. Furthermore, in an ordinary fracture both fragments remain alive since the well vascularized periosteum from without and the intra-osseous vessels from within guarantee enough protection. In a true intracapsular (subcapital) fracture of the neck of the femur the fragments have no periosteum, at least not the head. Secondly, it is generally agreed that after an intracapsular fracture the head of the femur dies, at least in most part. The head of the femur receives its main blood supply from intramedullary vessels running through the neck and from capsular arteries. The blood supply through the ligamentum teres, although active in younger individuals (Wolcott,³⁴ Chandler and Kieuscher⁸), is often inadequate in adults to maintain alone the viability of the head (Kolodny¹⁸). If a neck of the femur breaks intracapsularly the head of the femur is cut off from its main blood supply. Therefore, the head dies—at least most of it perishes. Such a fragment resembles a bone graft or rather, a transplanted epiphysis. Figure 4 d shows clearly the color difference between the well vascularized neck and the dead head. This femur is an autopsy specimen of an 81-year-old man upon whom I operated two days following the occurrence of the fracture, and who died 16 days postoperative from a cerebral thrombosis. The histologic examination of the head showed many of its osteocytes shrunk and many empty lacunae. Most of the articular cartilage, however, survived, protected as it was by the synovial fluid within the closed capsule. If the dead parts of such a head fragment become regenerated, the only way possible is by ingrowth of vessels and osteoblasts from the living parts of the neck across the fracture line into the head (Santos²⁶) or from the surviving osteoblasts. This process is assured only by complete and prolonged immobilization of both fragments, so that these delicate vessels can cross the fracture line un-

JOINT TRANSPLANTS

The specimens are autopsy specimens of patients operated on by the author. The pictures were taken with panchromatic and colored film (Kodachrome type A).

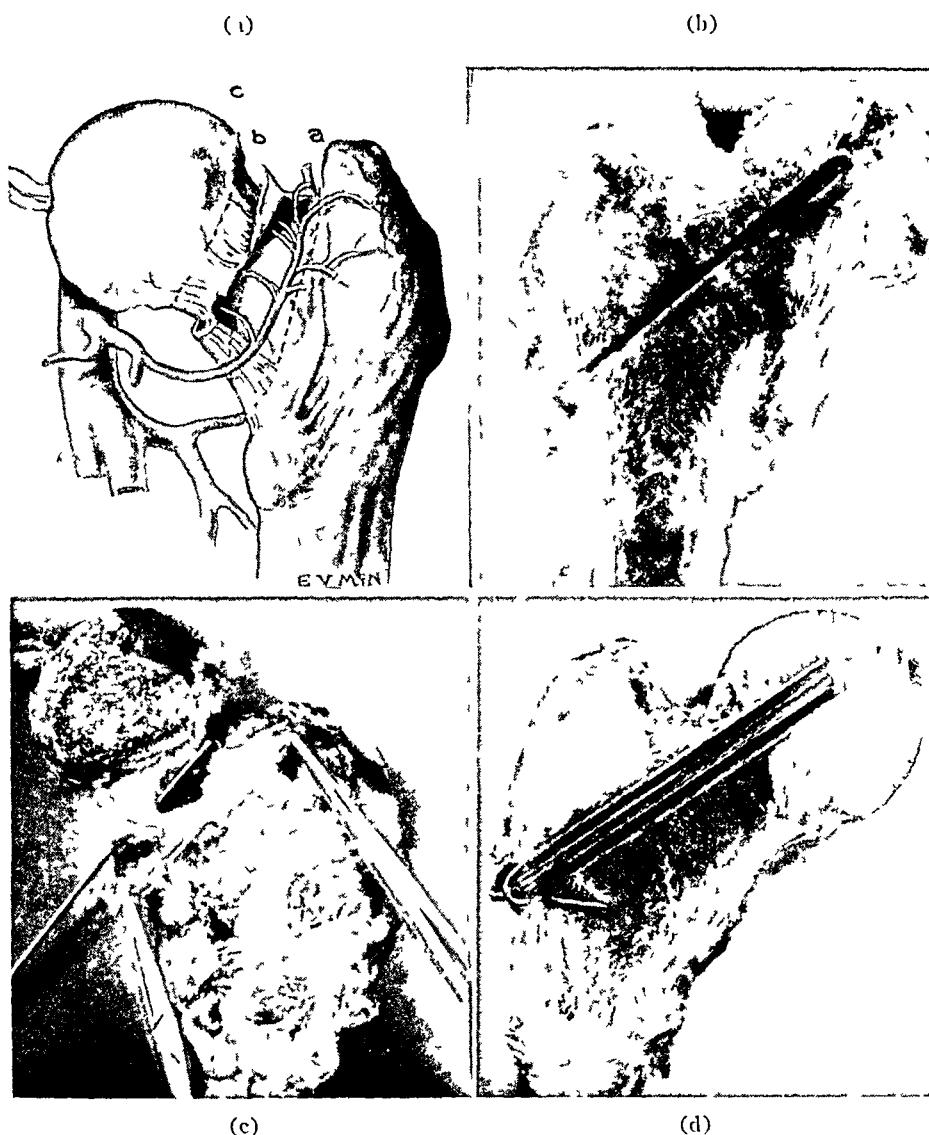


FIG 4(a)—Vascularization of the neck of the femur comes from three sources, intramedullary vessels, capsular vessels (branches of the art circumf femoris ant and post) and from vessels through the lig teres. The latter source is negligible in older individuals. In a fracture through line (a) both fragments remain vascularized. In a fracture through line (b) the upper half of the head fragment lies intracapsularly, the lower half extracapsularly, head fragment remains partially vascularized. In a fracture through line (c) the entire head fragment lies intracapsularly, becomes separated from its main circulation and is apt to die.

(b) Fracture through base of neck of femur (approximately through line (a) of Fig 4a). Both fragments remained vascularized (the dark areas are red on the colored film). This fracture had healed in seven weeks. Note the fibrous membrane which surrounded the nail and the marked hyperemia along it (foreign body reaction).

(c) Fracture through neck of femur, approximately through line (b) of Figure 4a. The upper half of the head fragment lies intracapsularly (the upper half of the capsule is severed) the lower half extracapsularly, hence the head fragment remains attached to the main circulation through the lower half of the capsule (note the strong vessel running parallel and close to left border of the capsule).

(d) True intracapsular (subcapital) fracture of neck of femur 16 days after operation 18 days after fracture, approximately through line (c) of Figure 4a. The head fragment is separated from its main circulation while the neck is well vascularized (the dark areas are red in the colored film). The head is pale and was found dead when examined microscopically. Note marked hyperemia in the living part of the neck of the femur along the nail. Layers of dense fibrous tissue were found along the nail canal in the same section of bone (foreign body reaction), but no such reaction was found in the dead head fragment. Hence a nail membrane developed only in the living part of the bone.

disturbed. Therefore impacted fractures always heal. But even under ideal conditions parts of the head may not become regenerated, particularly peripheral subarticular regions. They may break down on weight-bearing and lead to a deformity comparable with the "Mushroom" deformity of the Osteochondritis Juvenilis Deformans Coxae, a histological picture of which has been described by Peithes Axhausen, Phemister and others (H May²⁰). Hence complete prolonged immobilization by external or internal means is the most important factor in treating the true intracapsular fracture of the neck of the femur. If, due to incomplete immobilization, the vessels are prevented from crossing the fracture line, a nonunion may be the result. The following case may serve as an example.



FIG 51—Ununited fracture (pseudarthrosis) of the neck of the femur of five years duration. Note narrow curved fibrous disk running from "4" upward. Section of fibula had been transplanted 10 weeks previously. Marked hyperemia in and around the graft (the dark areas are red on the colored film).

(b) Microphotograph of a section of the fibula—graft and head of the femur (approximately of a region which is marked in Figure 5a). The graft and the host bone are in intimate connection. The graft (lower half of the field) as any other bone graft has died after the transplantation (note the disappearance of most of the bone nuclei), but there is evidence of transformation of the dead graft into living bone tissue—vascularization of the haversian canals, osteoblastic action particularly in the peripheral parts of the graft. The host bone is alive, its cells contain well stained nuclei; there is marked hyperemia and osteoblastic action. Note the row of osteoblasts lining the medullary space in the center of the field.

Case 3—A male, age 70, suffered a fracture of the neck of the femur. He stated that his injured leg was placed between two sandsacks, after five weeks he was allowed to sit in a chair, and after eight weeks to walk on crutches. His fracture did not unite, he limped and had pain on walking. Five years after the fracture he consulted me. Because the cleft between the fragments was narrow and, according to the roentgenograms, the head of the femur at least partially alive, a bone grafting operation was advised. I transplanted the middle section of the fibula without its periosteum into the neck of the femur, after Henderson,¹⁴ who uses a guiding wire and cannulated drills to make a proper-sized canal for reception of the fibula graft. The patient developed a postoperative psychosis and died ten weeks after the operation.

COMMENT—A thorough examination of his femur specimen led to the following conclusion. The original fracture was apparently intracapsular, with the exception of a small part of the head fragment, which remained

attached to the capsule and thus, to the circulation (Fig 5 a) It was reasonable to assume that this small attachment was not sufficient to maintain the entire circulation of the head fragment Circulation through the ligamentum teres was definitely out of the question in this case since it was found detached and shrunken Hence the greater part of the blood supply to the head fragment was severed leading to partial necrosis of this fragment Due to incomplete immobilization of the fragments, vessels and osteoblasts could not grow from the alive part of the neck in the partially necrotic head The result was a fibrous union To achieve a bony union the fibula transplantation was performed The grafted fibula died as any other bone graft does after transplantation Ten weeks after the transplantation, however, marked hyperemia and osteoblastic action could be found in and around the graft both in the section within the neck and within the head (Fig 5 b) From experience in operations on fractures of the neck of the femur and examinations of various specimens, I am inclined to believe that the true intracapsular (subcapital) fracture of the neck of the femur with necrosis of the entire head, as pictured in Figure 4 d, is the rare type It is this type of fracture in which regeneration may be incomplete or entirely absent, causing deformities of the head fragment or nonunion In most instances of fractures of the neck of the femur smaller or larger sections of the head fragment remain attached to parts of the capsule and thus to the circulation, saving at least some of the head from necrosis If such a head fragment is attached firmly upon the alive neck fragment by complete immobilization, it has a good chance to regenerate throughout and result in a bony union The main reason why the internal fixation (nailing, *etc*) of this type of fracture is more successful than any other treatment lies probably in the fact that it assures better immobilization of the fragments Even the large plaster encasement, no matter how well-fitting it may be allows slight movements of the fragments But internal fixation alone would not be successful were it not for prolonged avoidance of weight-bearing of the affected limb, to protect the dead bone from collapse and to assure immobilization In extracapsular fractures the fragments are covered by periosteum, second, the intra-osseous circulation of both fragments remains undisturbed (Figs 4 b and c), therefore, both fragments remain alive and such a fracture heals like any ordinary fracture and as quickly as any ordinary fracture no matter what kind of fracture treatment was employed

Another similar example is the healing process of a fracture of the capal scaphoid bone with death of the proximal half followed by bony union Most of the surface of this bone consists of articular cartilage leaving little room for active osteogenetic periosteum Hence its viability depends entirely upon intramedullary circulation From clinical experimental experiences (Watson Jones,³³ Oblatz and Halbshtein²¹) it is known that in about one-third of the cases the bulk of these vessels enters the bone on the distal (lateral) aspect of the bone and in the constricted midportion leaving the proximal (median) half supplied by the branches of the main vessels so that this part is rather

poorly vascularized (Speed²⁸) If, in such a case, a fracture occurs within the proximal half of the scaphoid or through the waist of the bone where the center vessels enter rupturing their trunks, the proximal half of the scaphoid is cut off from its circulation and dies (Fig 6) It may, however, become revived by ingrowth of vessels and osteoblasts from the viable distal half (Fig 7 a-d), provided absolute immobilization was carried out through the time of regeneration



FIG 6—Carpal scaphoid bone. Representation of its vessels and the relation between fracture lines and these vessels (After Böhler and Schnek⁵). A fracture through (a) will keep both fragments alive while a fracture through (b) and (c) will cause a necrosis of the median (lower) fragment

This type of regeneration apparently occurs in any intracapsular fracture in which one fragment has become separated from its circulation, followed by bony union

CONCLUSION—Certain intracapsular fractures do not heal like ordinary fractures. They heal in a manner similar to the regeneration of a transplanted epiphysis, namely, rather by bone regeneration and osteoconduction than by osteoproduction. The articular cartilage, however, remains alive, provided there is no delay in regeneration of the bony constituents (Campbell,⁷ Phemister²²)

SUMMARY

The processes involved in regeneration of joint transplants were discussed. These biologic processes were paralleled with those found in certain intracapsular fragments such as the head of the femur after a subcapital fracture and the median third of the scaphoid bone after certain fractures. A case of a fracture-dislocation of the humerus

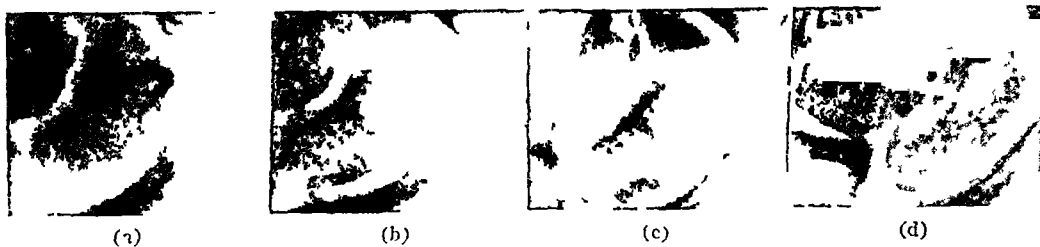


FIG 7a—Fracture of right carpal scaphoid bone (approximately through line (c) of Figure 6).
(b) Same fracture two months later. The distal (lateral) fragment is alive, the proximal (median) fragment is dead. The distal fragment had atrophied together with the other bones; the proximal fragment has remained dense because its calcium could not be carried away due to lack of vessels.
(c) Four months later the proximal fragment presumably has become revived.
(d) Six months later the fracture has healed.

was described in which the head of the humerus was reimplanted after temporary removal (autogenous half-joint transplantation). Another case of a 23-year-old patient was described in whom the upper third of the tibia, including the joint surface, was removed and replaced by a corresponding part of the tibia obtained from a 70-year-old man (homologous joint transplantation).

REFERENCES

- ¹ Albee, F H Restoration of Shoulder Function in Cases of Loss of Head and Upper Portion of Humerus Surg, Gynec, and Obstet, 32, 1, 1921
Idem The Treatment of Primary Malignant Changes of the Bone J A M A, 107, 1693, 1936
- ² Axhausen, G Die Nekrose des Proximalen Bruchstücks beim Schenkelhalsbruch und Ihre Bedeutung für das Hüftgelenk Arch f klin Chir, 120, 325, 1922
- ³ Behrend, M Transplantation of the Head and Shaft of the Fibula to the Humerus Surg Gynec, and Obstet, 51, 717, 1930
- ⁴ Bennett, G A, and Bauer, W A Study of the Repair of Articular Cartilage, etc Am Jour Pathol, 8, 499, 1932
- ⁵ Böhler, L Technik der Knochenbruchbehandlung Wien, W Maudrich, 1934 English trans ed by W Wood and Co, Baltimore, 1936
- ⁶ Burkle-de la Camp Die Untersuchungsbe funde von zwei Homoplastisch verpflanzten Kniegelenken Deutsch Ztschr f Chir, 217, 109, 1929
- ⁷ Campbell, W C Conservation of the Circulation in Bone and Joint Surgery Surg, Gynec, and Obstet, 58, 116, 1934
- ⁸ Chandler, S B, and Kreuscher, Ph H A Study of the Blood Supply of the Lig Teres and Its Relation to the Circulation of the Head of the Femur Jour Bone and Joint Surg, 14, 834, 1932
- ⁹ Dalla Vedova, R Ricerche Sperimentali Roma, 1911
- ¹⁰ Ducuing, J Contribution exp a l'etude des Greffes Articulaires Totales Paris, 1912
- ¹¹ Enderlen und Schmidt Über Transplantation von Leichenknochen Verhandl d deutschen pathol Gesellsch, 1914, p 314
- ¹² Gill, B A Transplantation of Entire Bones with Their Joint Surfaces ANNALS OF SURGERY, 61, 658, 1915
- ¹³ Haas, S L The Experimental Transplantation of the Epiphysis J A M A, 65, 1965, 1915
Idem The Transplantation of the Articular End of Bone Including the Epiphyseal Cartilage Line Surg, Gynec, and Obstet, 23, 301, 1916
- ¹⁴ Henderson, M S Ununited Fracture of the Neck of the Femur Treated by the Aid of the Bone Graft Jour Bone and Joint Surg, 22, 97, 1940
- ¹⁵ Impallomeni, G Sul Trapianto delle Articolazioni Arch di Ortoped, 28, 342, 1911
- ¹⁶ Judet, H Essai sur la Greffe des Tissus Articulaires Comp Rend Acad d Sci Par, 166, 193, 1908, *ibid* 166, 600, 1908
- ¹⁷ Klapp, R Über Umpflanzung von Gelenkenden Arch f klin Chir, 96, 386, 1911
Idem Chir-Kongr Verhandl, 1, 69, 1914
- ¹⁸ Kolodny, A The Architecture and the Blood Supply of the Head and Neck of the Femur and Their Importance in the Pathology of Fractures of the Neck Jour Bone and Joint Surg, 7, 575, 1935
- ¹⁹ Lexer, E Über Gelenktransplantation Chir-Kongr Verhandl, 2, 398, 1909
Idem Free Transplantation ANNALS OF SURGERY, 60, 166, 1914
Idem Joint Transplantation and Arthroplasty Surg, Gynec, and Obstet, 40, 782, 1925
- ²⁰ May, Hans Über Osteochondritis juvenilis deformans coxae Inaugural dissertation, Freiburg, 1926
Idem The Regeneration of Bone Transplants ANNALS OF SURGERY, 106, 441, 1937
- ²¹ Oblatz, B E, and Halbshtein, B M Nonunion of Fractures of the Carpal Navicular Jour Bone and Joint Surg, 20, 769, 1930
- ²² Phemster, D B Repair of Bone in the Presence of Aseptic Necrosis Resulting from Fractures, Transplantations and Vascular Obstruction Jour Bone and Joint Surg, 12, 769, 1930

- Idem* Fractures of Neck of Femur, Dislocations of Hip and Obscure Vascular Disturbances Producing Aseptic Necrosis of Head of Femur Surg, Gynec, and Obstet, 59, 415, 1934
- Idem* Bone Growth and Bone Repair ANNALS OF SURGERY, 102, 261, 1935
- Idem* Fate of Detached Articular Cartilage Tr Chicago Pathol Soc, 14, 245, 1935
- ²³ Portugolow, S Über Exstirpation der Oberen Hälfte des Oberschenkelknochens mit Vollständiger Autoplastischer Wiederherstellung der Extremität Arch f klin Chir, 184, 746, 1935
- ²⁴ Rehn, E, and Wakabayashi Die Homoplastische Transplantation des intermediärknorpels im Tierversperiment Arch f klin, Chir, 97, 1, 1912
- ²⁵ Rovsing, Th Et Tilfaelde af fri Knogletransplantation til Erstatning af Overormens Overste to Trediedele ved Hjaelp af Patientens Fibula Hospitalstidende, 53, 7, 1910
- ²⁶ Santos, J V Changes in the Head of the Femur after Complete Intracapsular Fracture of the Neck Arch Surg, 21, 470, 1930
- ²⁷ Skillern, P G Sarcoma of Humerus, Resection of Upper Shaft with Transplantation of Upper Third of Fibula to Humerus Stump Int Clinic Phila, 1, 41, 1920
- ²⁸ Speed, K Fractures of the Carpus Jour Bone and Joint Surg, 17, 965, 1935
- ²⁹ v Tappener, F H Studien zur Frage der Transplantationsfähigkeit des Epiphysenknorpels und des Gelenkknorpels Ztschr f d ges Exper Med, 1, 491, 1913
- ³⁰ Tietze, A Ersatz des Resezierten Unteren Radiusendes durch eine Grosszehenphalange Chu-Kongr Verhandl, 1, 77, 1902
- ³¹ Tuffier, M Resection Chondroplastique Bull et Mem Soc Chir, Mai, 492, 1901
- ³² Voronoff, L Traite des Greffes Humaines, Greffes Osseuses et Articulaires Paris, 1916
- ³³ Watson Jones, R, and Roberts, R E Calcification, Decalcification and Ossification Brit Jour Surg, 21, 461, 1934
- ³⁴ Wolcott, W E Circulation of the Head and Neck of the Femur J A M A, 100, 27, 1933

BRIEF COMMUNICATIONS

RAYABLE GAUZE¹

DEVELOPMENT OF A RADIOPAQUE, THREADED GAUZE SURGICAL SPONGE

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"With vivid words these just conclusions grace,
Much truth compressing in a narrow space,
Then many shall peruse, but few complain
And envy frown, and critics snarl in vain"

—PINDAR

It is undoubtedly true that human interest is centered more on *what* has been done than on *how* it has been done. Thus, the following short summary is drawn from long experimental studies, and is offered to make operative surgery safer for the patient.

Present methods and devices of sponge control have, thus far, failed to provide entire security against the accidental havoc of the "lost" sponge. Preventive measures and safety arrangements have been undone by the frailty and error within the human equation.

TABLE I

PREVENTIVE MEASURES DEvised FOR SPONGE CONTROL

(After Crossen and Crossen²)

1 SPECIAL ATTENTION BY OPERATING TEAM AIDS TO ATTENTION	4 MISC EXPEDIENTS STICK SPONGES
2 COUNTING SPONGES PRE-CLOSURE COUNT POST-CLOSURE COUNT AIDS TO COUNTING	5 CONTINUOUS SPONGE
3 ATTACHING TRACERS TAPE TO SPONGE	6 RAYABLE GAUZE METAL RING WIRE THREAD CHEMICAL IMPREGNATION FIBERGLAS THREAD

A specially prepared radiopaque thread is presented which embodies the qualities of marked radiopacity, relative chemical, physical and biologic inactivity, softness comparable to silk, and nominal cost of production.

It is suggested that in the manufacture of all surgical gauze that is to be used in the operating room, a single strand of lead "fiber-glas" thread might be incorporated into the gauze mesh, or so placed in prepared pads, sponges and gauze drain filler, that "lost" sponges can be more readily retrieved by roentgenographic identification.

Although such a radiopaque surgical gauze would not guarantee security against the losing of a sponge, by pointing to its presence and location it would mitigate the otherwise likely consequences of such an accident.

¹ Read before the Baltimore City Medical Society, Baltimore, Md., January 3, 1941.

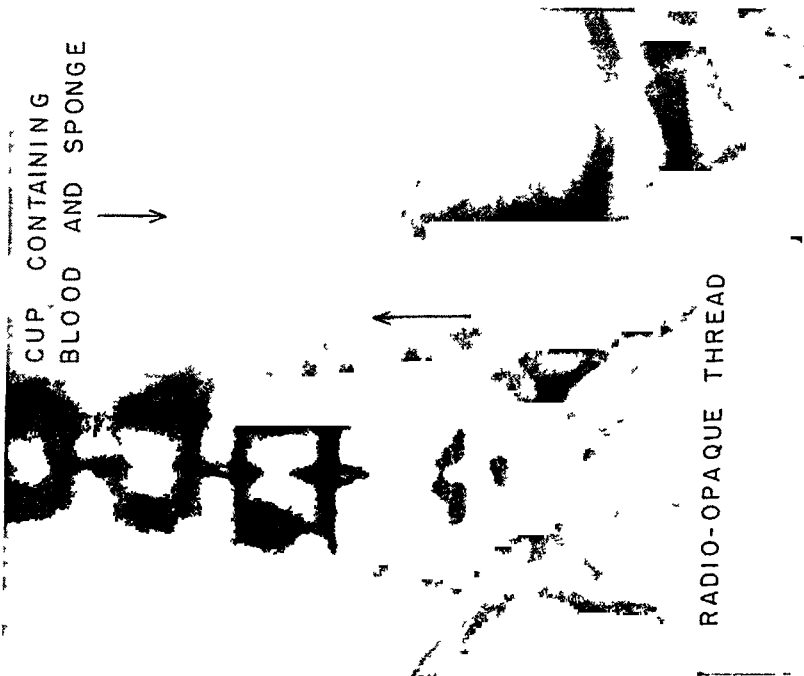


FIG 1—A "rivable" sponge placed in a cardboard cup containing 250 cc of citrated blood, and an abdominal film taken through an average sized person. The shadow cast indicates that blood cannot "black out" the opaque thread.

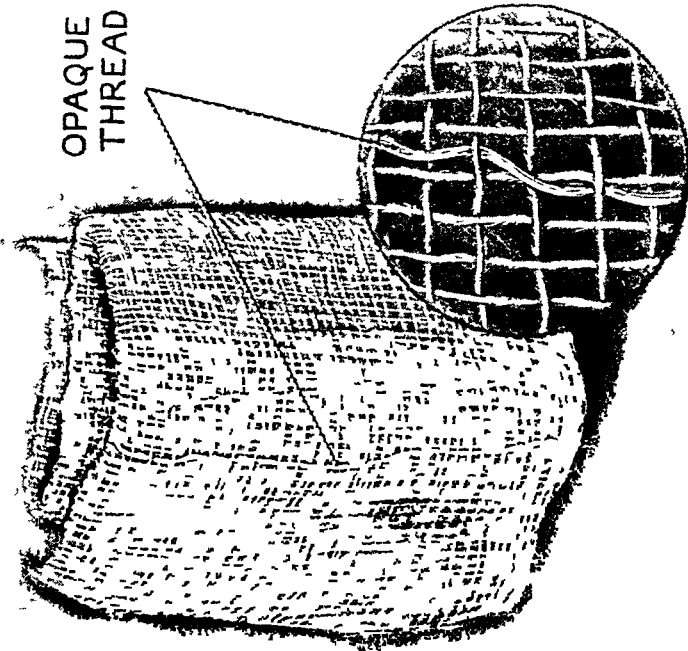


FIG 2—An artist's impression of "rivable" gauze. A single strand of thread is all that is necessary.



FIG 4—Roentgenogram of the right upper quadrant of an obese female. The "fiberglass" thread is contrasted with residual barium in the large bowel and a gallstone.



FIG 3—The elimination of the gauze foreign body in the pelvis and abdominal surgery can be accomplished by the use of a radiopaque threaded pad. The thread is clearly defined against the skeletal structures.

Rayable gauze fulfills the standards set by the American College of Surgeons, is applicable in every surgical situation, and is a comparatively inexpensive premium to pay for operating room security

REFERENCES

- ¹ Schachner, A Foreign Bodies Accidentally Left in the Abdominal Cavity ANNALS OF SURGERY, 34, 499-522, 678-702, 1901
- ² Kelly, H A What Precautions Shall We Take to Avoid Leaving Foreign Bodies in the Abdomen After Operations? New York Med Jour, 71, 405-407, 1900
- ³ Neugebauer, F Foreign Bodies Accidentally Left in the Peritoneal Cavity After Operation Report of 108 Cases Monatschrift Geburtsh u Gynak, 11, 821-844 1900
- ⁴ Crossen, H S Abdominal Surgery Without Detached Pads or Sponges Am Jour Obst, 59, 250, 1909
- ⁵ Greenhill, J P Foreign Bodies Left in the Abdomen After Operation Am Jour Obst, 25, 231-240, 1933
- ⁶ Crossen, H S, and Crossen, D F Foreign Bodies Left in the Abdomen C V Mosby Co, St Louis, 1940
- ⁷ Masson, J C An Extra Tag on the Abdominal Sponge J A M A, 72, 1612, May 31, 1919
- ⁸ Lewison, E F A Safe Surgical Sponge Surg, Gynec, and Obstet, 69, 694-696, 1939
- ⁹ Standardization of Surgical Dressings Bull Am Coll Surgeons, 24, 428-433, 1939

AN ATRAUMATIC FASCIAL-SUTURE NEEDLE

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IN 1901, L L McArthur¹ wrote his first article on a method of repairing herniae by the use of "living" fascial sutures. His described technic consists of splitting from the edge of the internal flap of the external oblique aponeurosis a one-eighth to three-sixteenths-inch strip of the white fibers which enter into the formation of the internal pillar of the ring. The strip is cut loose from its insertion in the muscle belly, but left attached at its inferior end to the spine of the pubis. A similar strip is taken from the outer flap, the lower end of which strip terminates in the fibers of the external pillar of the ring.

The operation is then completed according to the choice of the operator, either a Bassini or an Andrews procedure, using these strips as suture material for a running stitch.

His reasons for using his "tendon suture" were (1) Obtaining of a "living" suture which lies directly in the wound itself instead of requiring extensive dissections or abnormal displacements of important structures, (2) lessening the chance of failure through avoidance of introduction of dead or foreign tissue, (3) healing of the tissue *in situ*, rarely sloughing or becoming absorbed, and (4) incorporating of organized white fibrous tissue into the resisting cicatrix of the healed wound. When the fascial strips are loosened they roll up as does catgut, pull through as easily as catgut, and have a tensile strength of 11 to 24 pounds. He felt that the same procedure could be applied to other situations.

McArthur's technic gained little support from his contemporaries and was nearly lost in the mass of medical literature. It was not until about 20 years later that the use of fascial sutures was revived. In 1921, Gallie² became interested in the large number of ventral herniae found in soldiers who had been operated upon for abdominal wounds incurred during World War I, and in recurrent herniae of other types. He noted that, in most instances, the muscular and aponeurotic structures which had been sewn together in an attempt to close abdominal wall defects, due to extensive war injuries, had not remained firmly healed together, but had separated sufficiently to give rise to ventral herniae. Thus, he was led to the idea of closing these defects in the abdominal wall with free transplants of fascia lata strips woven into what he called an "aponeurotic filigree." He then demonstrated that these strips, when placed in such a position that they received an adequate supply of lymph, continued to live unchanged.

After conventional suture operation for inguinal hernia with recurrences, in no case did Gallie find any evidence of adhesion between the conjoined tendon and the inguinal ligament, stating that "From our clinical experience, therefore, and from the information derived from our experience, we have come to the conclusion that operations designed to produce permanent adhesion between aponeurotic structures having a natural tendency to separate are defective in principle, if they depend solely upon the process of healing in the line of suture. Herein lies the explanation of the high percentage of recur-

rences in large ventral herniae and in indirect inguinal herniae, even when the operations have been performed by the most competent hands" Therefore, Gallie began using transplants of fascia lata as living sutures which might permanently hold the edges of hernial rings together without depending upon the natural process of repair Gallie, using fascia lata strips, corroborated McArthur's findings that a living suture had the great advantage over catgut and similar sutures, in that it was not absorbed but continued to perform the function for which it was originally intended Over silk and other nonabsorbable sutures it was superior in that it being composed of a perfectly nonirritant



FIG 1—Head of the needle unscrewed, note the gaping jaws (X2)

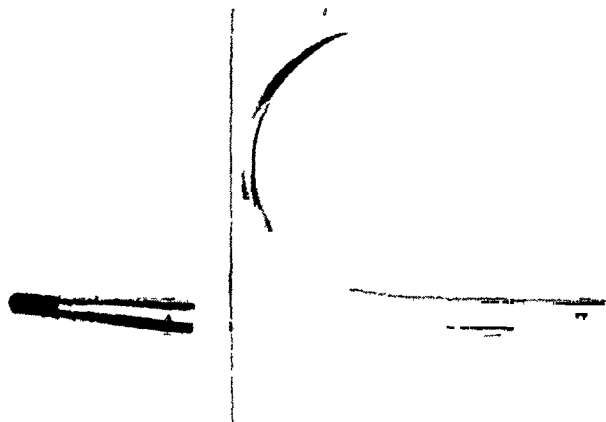


FIG 2—Head partially screwed into the shaft Jaws now partially closed (X2)

living tissue, healed solidly into the tissues through which it passed He, furthermore, demonstrated that it did not show a tendency to cut-out when subjected to any normal physiologic strain

One of the chief technical difficulties in the use of fascial sutures has been the lack of a suitable needle to draw the fascial strip through the tissues with the least possible trauma McArthur tied a strand of No 3 silk (with a single knot) tightly to the free end of the strip of fascia, threaded the silk into an ordinary needle, and then pulled the fascial suture through the tissues to be united In using this technic it is apparent that the operator would encounter difficulty in drawing the suture through so firm a structure as the aponeurosis of the external oblique, or through the inguinal ligament

Gallie threaded the fascial suture into a needle with a large eye (so-called Gallie needle) He then tied the strip of fascia securely into the needle with catgut or silk to prevent its unthreading, and tied a ligature of catgut around the terminal end to prevent it from splitting In taking the first stitch, he recommended that the needle be passed through one of the edges of the gap to be closed and through the terminal end of the suture, and drawn taut—thus producing a sort of slip-knot to anchor the fascial strip He ended the suture by splitting the terminal end, and tying the two strands thus produced about itself in a triple knot This knot was made secure by transfixing it with a catgut ligature, to hold the loops together until they became firmly healed

Gallie's technic of attaching the fascial suture into a large-eyed needle was

an improvement in that the semicutting-edged curved needle started a small rent in the aponeurosis through which the suture could be pulled. But it is obvious that the fascial suture was, of necessity, of double thickness at the point where it was threaded through the eye, and that this double thickness produced undue trauma when it was forced through the tissues.

In an attempt to overcome this difficulty I devised a comparatively atraumatic needle. Basically, it is a semicutting-edged, curved, two-pieced needle of approximately the same size as the so-called Gallie needle. The distal section, about three-quarters the length of the entire needle, consists of a triangular semicutting edge on a curved shaft. At the proximal end of this section is a female thread which has been longitudinally countersunk to a depth of about one-quarter inch, the countersinking being of the greatest possible diameter consistent with the strength of the spring steel shaft. Into this screws the short proximal section which, manufactured out of a specially tempered spring steel, is of the same diameter as the rest of the needle, except that its proximal two-thirds is hollowly slit longitudinally down the middle, and its distal half tapers down to a male screw of much less diameter. When unscrewed, this section gapes open, but when screwed into the shaft of the distal section the tapering fits tightly into the countersinking and the gaping ends are forced together.

In use, the end of the fascial suture is placed between the gaping ends of the head of the needle, and the head screwed into the shaft. The squeezing pressure of the split ends coming together retains the suture in the needle. As a further aid to holding the suture in place, a tiny pin is incorporated at right angles into the medial surface of one side of the split. This pin digs at right angles into the suture when the head is tightened.

The result is a streamlined needle-fascial-suture junction. The fascial suture may now be pulled through the fibrous tissues of the aponeurosis, inguinal ligament, and conjoined tendon with no more trauma than that which is caused by the needle alone. The diameter of this needle is about three-sixteenths inch, just large enough to be attached to the most commonly used fascial suture strips which are one-eighth to three-sixteenths inch in width.

This needle has another advantage, in that it can be used repeatedly. Furthermore, it may also be attached to kangaroo tendon sutures, ribbon-gut, and for suture materials of similar types.

SUMMARY

(1) A brief résumé of the history and uses of strips of living fascia as suture material has been given.

(2) Some of the advantages of fascial sutures over conventional sutures in the repair of various types of herniae have been described.

(3) The author has described an atraumatic needle of simple design, which may be used to facilitate the use of fascial and other large caliber sutures.

REFERENCES

- ¹ McArthur, L. L. JAMA, 37, 1162, 1901
Idem JAMA, 43, 1039, 1904
- ² Gallie, W. E., and LeMesurier. Canad. Med. Jour., 13, 469, 1923
Idem Arch. Surg., 9, 516, 1924

A PUNCH FOR CUTTING COTTONOID SPONGES FOR USE IN NEUROSURGICAL OPERATIONS

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GENTLE MANIPULATION of nervous tissue is of even greater importance in neurosurgical procedures than in most other types of surgery, because irreparable injury to the brain or spinal cord may be easily produced. Circular cottonoid pledgets and rectangular strips of some other nontraumatizing material are indispensable for sponging nerve tissue and for protection under retractors. As sponges, the moist, circular pledgets readily absorb blood and cerebrospinal fluid, due to enormous capillary surface afforded

by the fibrils. Application of the suction tip directly to the pledget overlying the bloody surface rather than directly to the tissue prevents injury by the suction tip and facilitates suction by obviating clogging of the instrument. In addition, the capillarity of the pledget is effective in permitting the entire field it covers to be cleansed, although the suction tip is applied to but one point on the pledget.

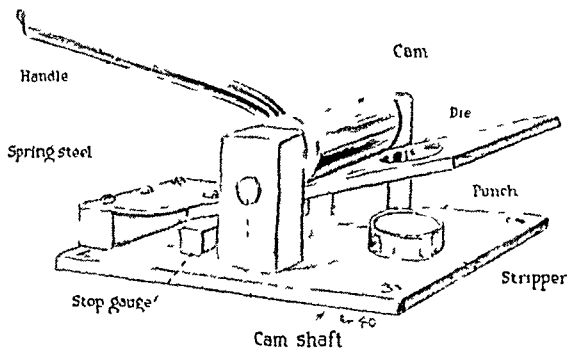


FIG 1—View of punch showing relation of cam shaft to cam when not in operation. The handle is pictured shortened in order to conserve space.

In the long, painstaking procedures involved in such operations as brain tumor removals, over 200 circular pledgets may be used. These are usually of two diameters: (1) About three-quarters of an inch, and (2) about one-half or three-eighths of an inch. Cutting these out by means of scissors is a tedious and tiring procedure.

In the operating rooms at the University of Minnesota Hospitals, two punches for cutting the circular cottonoid pledgets are in regular use—one cutting smaller, the other cutting larger sponges. Both punches, one of which is shown in Figure 1, are mounted on a single, heavy iron casting, for stability during stamping. The punch assembly consists of the circular punch proper, mounted on a base $4\frac{1}{2} \times 4 \times \frac{1}{2}$ inches, a die plate mounted on a flap of spring steel, and a cam actuating the die plate and operated by a handle about ten inches long. The cam shaft is eccentrically mounted, permitting gradual downward movement of the die on the punch as the arc described by the handle increases. An iron stop-gauge limits the descent of the die plate. A segment of thick rubber tubing slipped over the punch and allowed to project slightly above it serves as a stripper.

The exact dimensions of the apparatus are indicated in the work diagrams. Figures 2A and 2B. Figure 2A is a side elevation and Figure 2B is a front

elevation, the die plate (D Pl) and punch being shown engaged with the stripper compressed. In this position, the handle is nearly parallel to the base. The cam shaft mounting requires no lubrication, but friction between

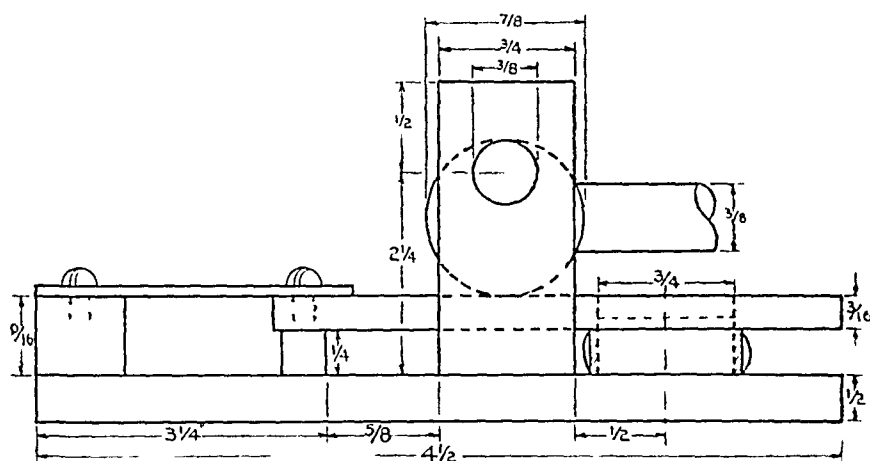


FIG 2A

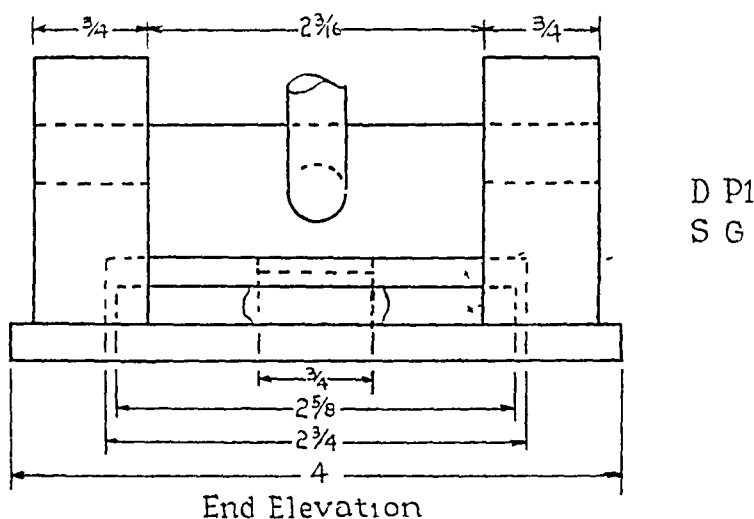


FIG 2B

FIG 2—Work diagrams of punch in stamping position (A) Side elevation (B) End elevation D Pl die plate S G stop gauge

the cam and the die plate can be minimized by a light coating of machine oil. The moving parts of the apparatus are sturdy, requiring no replacement. The punch and die are made of high carbon steel so that necessity for sharpening is eliminated. A single punch assembly can be made for approximately seven or eight dollars.

In operation, a large sheet of cottonoid is passed between the punch and die plate, and pledgets are stamped out from each fresh area at the rate of about 60 per minute.

SUMMARY

An inexpensive punch is described for stamping out circular cottonoid pledgets used as sponges in neurologic surgery. The ease and rapidity of operation results, primarily, from a minimum of movable parts.

Appreciation is herewith extended to Mr. John A. Phelan of the University of Minnesota Scientific Apparatus Shop, for his wholehearted cooperation in the construction of this punch and preliminary experimental devices.

BOOK REVIEW

Annals of Surgery
August 1942

A MANUAL OF THE TREATMENT OF FRACTURES By John A. Caldwell, M.D. Charles C. Thomas Co., 1941

A Manual of the Treatment of Fractures, written in a plain and simple text, by a Professor of Clinical Surgery, for students and interns, and dedicated to the House Officers of the Cincinnati General Hospital, is offered by the publishers

With such a clear statement of its objectives, this manual should create an unusual amount of interest among such groups, and to a far greater number of men represented by the general practitioners

The need for such a Manual has long been recognized, and this contribution of Dr. Caldwell's meets it, as would be expected from such a master surgeon. The fact that the author is a general surgeon, and Director of the Fracture Service of the Cincinnati General Hospital, qualifies him to speak upon this subject.

His experience is evidenced throughout the text by such statements as

"The use of local infiltration anesthesia for the reduction of fractures"

"The most useful form of splinting material is plaster of paris"

"It is always a serious mistake to administer an anodyne to relieve pain or discomfort caused by splints"

"Ascertain beforehand if the patient is serum sensitive before giving antitetanic or other forms of sera"

His reference to the Orr treatment in compound fractures instead of the more complicated technic of Dakin-Carrel, is now generally accepted.

The use of line drawings for illustrations instead of the usual reproduction of roentgenograms and photographs is an innovation which should be commended.

It is unnecessary to say that such a book is timely, in the face of the increasing demands now being made by military, industrial and automobile accidents.

WALTER ESTELL LEE, M.D.

EDITORIAL ADDRESS

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SYMPOSIUM ON INTESTINAL ATRESIA



INTESTINAL OBSTRUCTION IN THE NEWBORN

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SURGICAL TREATMENT of congenital obstruction of the intestine in the newborn is at last beginning to produce encouraging results. Thirty years ago, not a single successful operation had been announced, and most cases had been described only as autopsy findings. More recently, a small but gradually increasing number of recoveries has been reported. To Dr William E. Ladd, Dean of pediatric surgery in this country, must go most of the credit for the achievements of surgery in this new field. Not only has Doctor Ladd called attention to the prevalence of this condition and stimulated efforts at making early diagnoses, but he has made valuable contributions to the operative technic and developed an original operation for relief of the extrinsic type of obstruction. The subject is presented in detail by Doctors Ladd and Gross in their recent volume entitled "Abdominal Surgery of Infancy and Childhood." Their discussion of congenital obstruction is based on a series of 118 cases treated in the Boston Children's Hospital, with 44 recoveries. The extent of this experience, however, is unique, and a search of the literature on the subject shows only reports of single cases or small groups. We feel justified therefore, in reporting our own group of six cases, five of which were operated upon, with three recoveries.

Congenital obstruction of the intestine should be suspected whenever a newborn baby begins vomiting persistently soon after birth. The vomitus is usually bile-stained. It quickly becomes projectile, and everything taken by mouth is promptly lost if the obstruction is complete or almost so. The site of the obstruction cannot be predicted by the time-interval between birth and onset of vomiting, since the entire intestinal tract above the obstruction is already distended at birth by digestive juices and swallowed amniotic fluid. When air and fluids are swallowed in the first feeding efforts, distention is further increased and vomiting results. When obstruction is incomplete or intermittent vomiting may begin later and may be less persistent, making diagnosis more difficult.

Anatomically considered, congenital obstruction may be intrinsic or extrinsic. The intrinsic obstruction is more frequent and may occur at any

location. It results from failure of reestablishment of the bowel lumen during the early weeks of fetal development. Proliferation of epithelium obliterates the lumen of the primitive gut for a time, but normally the lumen reappears after confluent vacuolization of the central mass. If this process is incomplete, one or more septa may remain to block the lumen or sections of the intestine may be represented by solid fibrous cords or threads. The condition is known as atresia when the bowel lumen is completely obstructed or when there is loss of continuity and as stenosis when a small but ineffective opening is present. In either group, the clinical picture is essentially the same, though in stenosis the abnormalities are more likely to be amenable to surgical treatment.

Extrinsic obstruction usually is a result of incomplete rotation of the colon associated with abnormally placed folds or bands of peritoneum which most frequently impinge upon the lower half of the duodenum.

Diagnosis of congenital atresia or stenosis can often be made on the history alone. In the absence of intracranial birth injury or unusual infection, bile-stained projectile vomiting beginning soon after birth and persisting, almost invariably means obstruction of the intestine. Hypertrophic pyloric stenosis can be differentiated by the later onset of vomiting and absence of bile from the vomitus.

Positive diagnostic aid may often be obtained from roentgenologic studies. Plain films of the abdomen are usually adequate, outlining the gas-filled obstructed stomach and intestine with striking clearness. Barium may be given if necessary but is to be avoided if possible because of danger of vomiting and aspiration into the lungs, and because masses of barium, difficult to remove by lavage, may interfere with operative procedures.

Survival of infants with complete obstruction depends on early diagnosis, and immediate repair of the defect. Without surgery, death invariably occurs within a week or ten days when obstruction is complete, and high degrees of partial obstruction are very poorly tolerated. Close coordination of medical and surgical care is an essential factor in survival. There is often jaundice with consequent bleeding tendency, which must be combated with vitamin K. Treatment of metabolic disturbances, especially dehydration, require pre-operative administration of fluids and blood transfusion. Ether anesthesia is preferable because of relaxation needed for adequate exploration. An incision of considerable length is advisable to facilitate the extensive operative procedure often necessary. In cases of intrinsic obstruction, the best chance of a favorable outcome is offered by the performance of a primary anastomosis about the site or sites of obstruction. Two-stage procedures are poorly tolerated. In extrinsic obstruction, Ladd has demonstrated that the most satisfactory results are to be obtained by releasing the peritoneal band lying across the duodenum and reducing the volvulus of the small intestine often associated with this lesion. Certain important details of surgical procedure are essential to success in operations on these tiny patients. Body heat must be preserved and any appreciable change in temperature avoided. The delicate

tissues must be handled with extreme gentleness and complete hemostasis obtained. Postoperative care should include transfusion with whole blood or plasma, and care to avoid vomiting and distention by use of lavage and suction.

The following case reports include five intrinsic obstructions and one of the extrinsic type. Of the intrinsic group, one, which had a jejunal atresia, died before operation could be attempted. Two others with jejunal

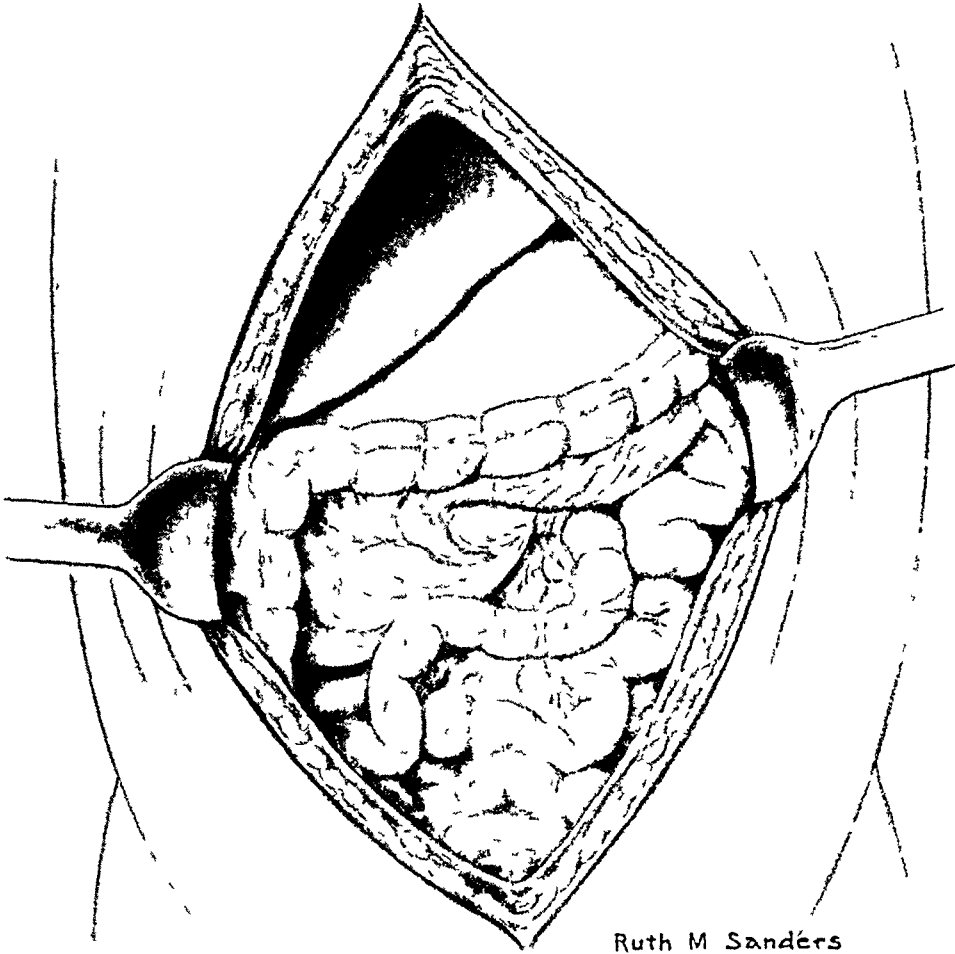


FIG. 1.—Case 1. Stenosis of duodenum near duodenojejunal junction. Findings in Case 6 were identical.

atresia were operated upon unsuccessfully, one dying 17 days after operation and the other 12 days postoperative. Both of these children had defects of the intestinal tract which were so extensive that physiologic function could not be restored, although satisfactory anastomoses were provided. Both of the cases of duodenal stenosis survived operation and are apparently developing normally, as is also the single case of extrinsic obstruction, upon which the Ladd operation was performed.

CASE REPORTS

Case 1—Baby E, a white female, was born at Baylor Hospital, 2 00 A M July 6, 1938 Full term Normal delivery Birth weight Six pounds, four ounces Mother had hydramnios Nursed with some difficulty but did not vomit for 48 hours after birth One small stool of meconium passed Vomiting became frequent and was bile-stained

Physical Findings Normal except for moderate abdominal distention and occasional visible peristaltic waves from left to right in the upper abdomen

On July 8, 1938, a plain roentgenogram showed stomach and duodenum moderately distended with gas Next day, barium was given and definite evidence of obstruction of duodenum obtained Weight Five pounds, five ounces *Clinical Diagnosis* Congenital obstruction of duodenum

Operation—July 10, 1938 Under ether anesthesia, a right upper rectus incision was made, through which the upper abdomen was explored The stomach and duodenum were found to be greatly dilated and thick-walled It was apparent that the obstruction of the lumen was due to an intrinsic defect, such as a persistent diaphragm The jejunum and large intestine were normal in appearance wherever seen The liver was normal (Fig 1)

A short-circuiting operation was performed, anastomosing the side of the third portion of the duodenum with the side of the proximal end of the jejunum A rent was made in the mesocolon, through which the wall of the duodenum was brought and attached by stay-sutures of No 0000 chromic catgut to the antimesenteric border of the jejunum as near as possible to its origin An anastomosis, with a stoma about two centimeters long, was made, using two layers of No 0000 catgut sutures on atraumatic needles When the duodenum was opened, a catheter was passed upward into the stomach, meeting no obstruction, and was then passed downward to the point of obstruction at the base of the mesocolon Wound closed with continuous fine catgut suture in the peritoneum, interrupted figure-of-eight A-silk sutures in the anterior rectus sheath, and interrupted A-silk sutures in the skin *Postoperative Diagnosis* Congenital stenosis of duodenum

Postoperative Course CO₂ and O₂ were administered 24 hours to combat cyanosis Transfusion, saline and glucose given parenterally Water one ounce every hour was started after 12 hours, and most of it retained On third day, dilute breast milk was started, and the baby vomited small amounts twice After this, there was no vomiting, and she was fed from the breast, gaining weight steadily Discharged with mother, July 26, 1938, 16 days after operation Weight Five pounds, 15 ounces The wound healed firmly, although there was a delay of three weeks in the healing of the skin edges

This child has been seen at frequent intervals since operation Her development has been entirely normal in every way, and she has enjoyed excellent health

Case 2—Baby W, white male, was admitted June 1, 1941 Born 2 45 A M May 29, 1941 Twenty days premature Birth weight Six pounds, eight ounces Had vomited everything taken since birth No bowel movements On admission, weight five pounds, four ounces Moderate dehydration Slight jaundice Lungs clear and fairly well expanded Heart sounds clear No murmurs Tick-tack rhythm Abdomen slightly distended, soft No masses palpable No visible peristalsis Urine normal Hb 64 per cent R B C 3,950,000 W B C 8,000 P M N 38 Prothrombin time five minutes Kline negative No stool passed After gastric lavage, a thin mixture of barium was given Fluoroscopy and roentgenograms showed esophagus and stomach to be greatly dilated and beneath these a large V-shaped shadow, probably representing duodenum and upper jejunum, also greatly dilated

Course in Hospital Fluids and glucose were given parenterally Nothing by mouth was allowed Transfusions were given No stools were passed other than a few particles of greenish material, which contained no bile Vitamin K was given, and

prothrombin time was lowered to one and one-half minutes *Clinical Diagnosis* Congenital atresia of the small intestine

Operation—June 3, 1941 Under light ether anesthesia, a right paramedian incision was made. Almost the entire abdominal cavity was occupied by the dilated stomach, continuous with an enormous loop of distended small intestine. The exact identity of this loop could not be determined, although it had the appearance of a greatly enlarged

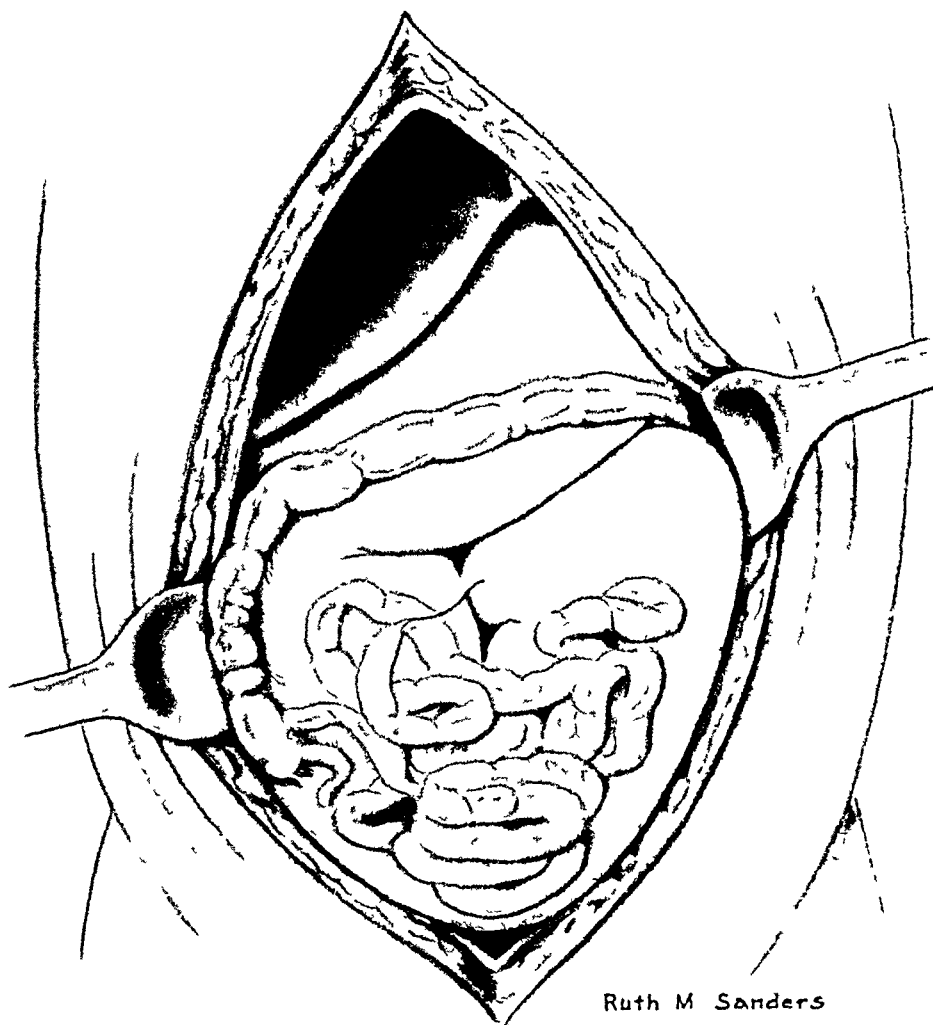


FIG. 2—Case 2. Atresia of jejunum and abnormal attachment of ascending and transverse colon.

duodenum, extending downward in the right side of the abdomen into the pelvic cavity and up the left side under the diaphragm then medially to end blindly in the usual location of the duodenojejunal junction. Here the intestine was replaced by a fine fibrous cord three centimeters in length which joined the dilated portion and the beginning of a normal looking small intestine, completely collapsed. The cecum, appendix, and ascending colon lay loosely adherent to the anterior surface of the descending limb of the dilated loop. The large intestine was collapsed but normal in appearance as far as it could be traced to a point where it was concealed by the ascending portion of the dilated loop. The liver and gall bladder were normal in appearance (Fig. 2).

An anastomosis was made between the distal end of the dilated intestine and the collapsed jejunum near its proximal end. Two layers of No. 00000 chromic catgut were

used The abdominal wound was closed with through-and-through silk sutures *Post-operative Diagnosis* Congenital atresia of the jejunum, abnormal attachment of ascending colon

Postoperative Course Given concentrated blood plasma intravenously immediately after operation Condition was good for several days Nothing was given by mouth for 48 hours, then water in small amounts was given but vomited immediately Vomiting continued, no stools were passed Normal saline solution was injected into the lower bowel and promptly expelled Prostigmine caused audible peristaltic activity for a few minutes but no stool resulted Temperature remained constantly subnormal Upper respiratory infection appeared Death occurred at 12 45 P M June 20, 1941 Autopsy permiss on was refused

Case 3—Baby N, a white female, was admitted, June 11, 1941, 12 hours after birth Birth normal Full term Weight Four pounds, six ounces Mother had polyhydramnios Baby began vomiting immediately after birth and this continued at frequent intervals until death No stools were passed The baby's body had felt cold and on admission temperature was 97.8°, falling later to 96.4° Aside from the small size and low temperature, there were no abnormal physical findings

Urine Albumin—a trace, rare W B C, and casts Hb 20.8 Gm R B C 5,800,000, W B C 9,600 P M N 39 Prothrombin time six minutes Kline negative

Course in Hospital Small amounts of greenish fluid were vomited frequently, although the stomach was lavaged repeatedly and nothing given by mouth for 24 hours A weak milk formula was then given and promptly vomited Transfusions and intravenous saline and glucose were given On the third day, a few particles of greenish material were passed from the bowel On June 15, 1941, four days after birth, the child died, with a sudden rise of temperature to 104° The probable diagnosis was "birth injury" No surgical consultation had been requested

Autopsy Report—Anatomic Diagnosis

- 1 Congenital abnormalities of gastro-intestinal tract
 - a Lack of continuity of duodenum and jejunum
 - b Marked dilatation and distention of duodenum, stomach, and esophagus
 - c Partial atresia of jejunum
 - d Small ascending, transverse, and descending colon
 - e Absent omentum
- 2 Prematurity
- 3 Fetal atelectasis
- 4 Small right ventricle
- 5 Patent ductus arteriosus
- 6 Mild icterus
- 7 Uric acid infarcts of kidneys

"On making the usual midline incision, there is a very thin layer of granular fat present in the abdominal wall The peritoneal surfaces are smooth and glistening throughout, and there is no excess of fluid A markedly dilated loop of intestine presents itself, and this is later identified as markedly dilated duodenum The stomach is properly rotated in its correct location, it is markedly distended with gas The constriction of the pylorus is readily identified From this point onward, the duodenum is markedly distended, and in this manner has displaced the remainder of the gastro-intestinal tract downward The first portion of the duodenum is attached to the visceral surface of the liver by means of peritoneum, from this region the duodenum pursues its usual U-shaped course to the left, being related to the right kidney and suprarenal gland It ends as a blind pouch without any connections to the jejunum No atretic connection can be made out The jejunum commences as a blind pouch of fair size, and this is connected to the remainder of the jejunum by means of a fibrous cord, this pouch is entirely separated from the duodenum, and the two lumina are not continuous The remainder of the jejunum and ileum are of the usual appearance, the appendix is in the

BOWEL OBSTRUCTION IN THE NEWBORN

right lower quadrant The entire colon appears to be much smaller than usual, the transverse portion is enveloped by the visceral peritoneum of the duodenum and stomach There is no omentum present (Fig 3)

"On opening the chest, the lungs fill their respective spaces, there are no adhesions The pleural surfaces are smooth and glistening, and there is no excess fluid The thymus gland is not enlarged, is bilobed and composed of soft, grayish tissue

"On opening into the pericardial sac, no excess fluid is present, and the surfaces are smooth and glistening The superior and inferior venae cavae are markedly distended

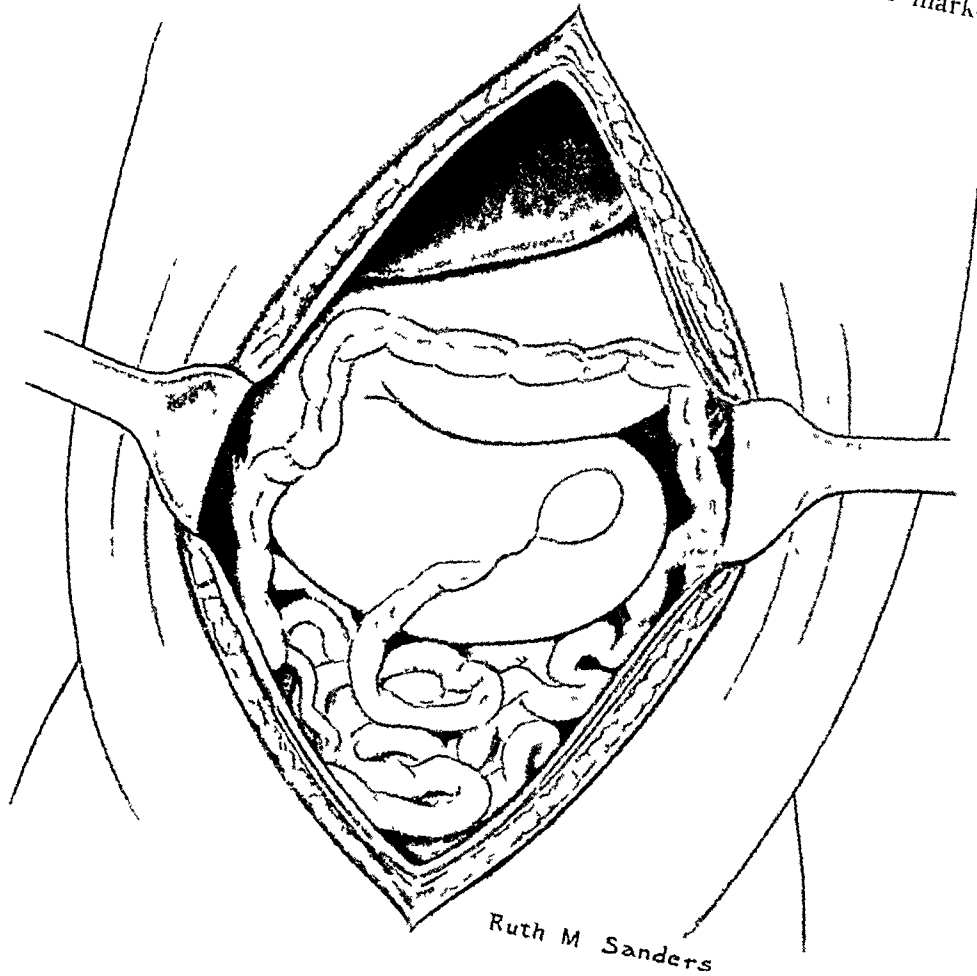


FIG 3—Case 3 Atresia and aplasia of jejunum

with blood The heart is of normal size, and there are no abnormalities about the aortic arch or its main branches

"Both lungs float in water The right lung is trilobed and of dark reddish-purple color, it fails to crepitate and is flabby The larger bronchi are of the usual caliber and are not obstructed On section, the cut-surface is dark red in color, and a minimal amount of air can be expressed The left lung is bilobed and resembles its fellow in all respects

"The left auricle of the heart is empty, and the foramen ovale is functionally closed The chamber of the right ventricle is much smaller than usual, there are no abnormalities about the tricuspid valve The cusps of the pulmonary valve are intact There are no changes noted about the mitral or aortic valves The myocardium is deep red in color and of good tone"

Case 4—Baby M, a colored female, was admitted June 28, 1941. Born 1 00 A M June 27, 1941. Full term. Normal delivery. Had received nothing by mouth except water in small amounts, and had vomited greenish fluid persistently. There had been no bowel movement. Weight Five pounds, eight ounces. Except for slight dehydration, physical examination was normal. The abdomen was soft, and no masses were felt.

Urine contained albumin, and a rare pus cell. Hb 11 Gm RBC 3,000,000 WBC 8,000 PMN 98 Kline negative.

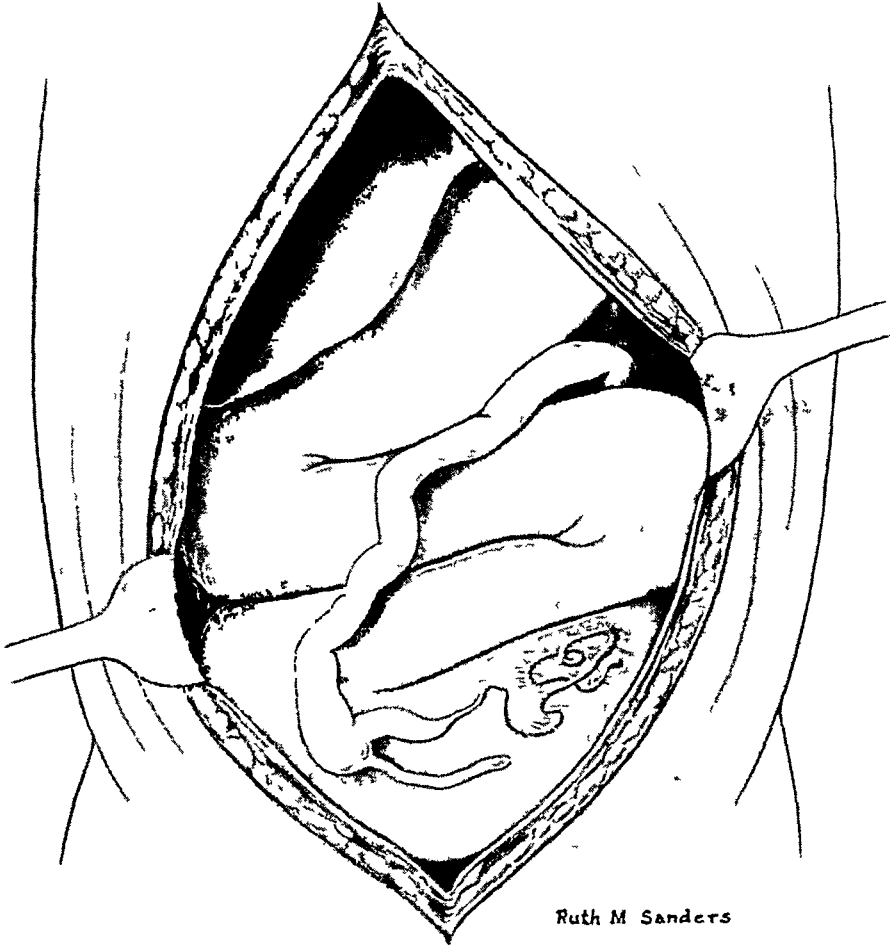


FIG 4—Case 4 Atresia of jejunum and aplasia of ileum. Abnormal attachment of ascending and transverse colon.

After oral administrations of barium, roentgenograms showed a great dilatation of the stomach and upper part of the small intestine, which were partly filled with barium. Below this, was more gas-filled intestine. Barium enema showed a small but normal appearing colon.

Course in Hospital Nothing was given by mouth, but vomiting continued. Saline and glucose were given parenterally as well as blood transfusion. Vitamin K was given in preparation for operation. *Preoperative Diagnosis* Congenital obstruction of small intestine.

Operation—June 30, 1941. Under light ether anesthesia, a right paramedian incision five centimeters long, was made. The abdominal cavity was almost entirely filled by a

large sac-like dilatation of stomach and upper part of the small intestine. The first impression was that the main part of the cystic mass represented a huge dilated and hypertrophied duodenum, but closer inspection showed transverse folds dividing the mass into a series of three loops, closely pressed together and adherent. This dilated portion of the small intestine ended blindly in the left lower quadrant of the abdomen, and the remaining portion of the small intestine was represented by a small, twisted cord-like structure intimately adherent to the anterior surface of the terminal dilated loop. The cord connected with the proximal end of a very short terminal ileum, six centimeters in length, which was of normal diameter and possessed a lumen. The cecum, appendix and ascending colon were small and collapsed, and lay on the anterior surfaces of the dilated loops of small intestine, running upward to the right of the midline to disappear under the greater curvature of the stomach. The wall of the dilated intestine was thick, slightly edematous, and hyperemic (Fig. 4).

An anastomosis was made between the side of the short terminal ileum and the blind end of the dilated intestine. Two layers of No. 0000 chromic catgut were used. The abdominal wound was closed with through-and-through C-silk sutures. *Postoperative Diagnosis:* Congenital atresia of jejunum, aplastic ileum.

Postoperative Course: Operation completed with no apparent shock. Concentrated blood plasma given intravenously. Stomach was lavaged repeatedly, and nothing given by mouth for three days. Vomiting continued, but less frequently. Saline solution was injected into the rectum to stimulate bowel activity but no stool was passed until the seventh postoperative day, when a few shreds of greenish material were expelled. Similar scanty stools were passed several times thereafter. After the third day, weak glucose solution and, later, an evaporated milk formula were given by mouth, but vomiting continued. Transfusions and parenteral fluids were given daily. Jaundice developed, followed by upper respiratory infection. Death occurred, July 12, 1941, on the twelfth postoperative day.

Autopsy Findings—Anatomic Diagnosis

- 1 Congenital atresia and aplasia of ileum
- 2 Marked dilatation of jejunum and duodenum
- 3 Surgical anastomosis of terminal ileum and jejunum
- 4 Marked jaundice
- 5 Chronic fibrous adhesions in peritoneal cavity
- 6 Slight diminution in rotation of colon
- 7 Patent ductus arteriosus
- 8 Patent foramen ovale
- 9 Confluent bronchopneumonia of both lungs

"The fat in the midline is deep yellow in color. On opening into the peritoneal cavity, the loops of the intestine are markedly adherent by fibrous tissue. There are several markedly distended loops of small intestine. The stomach and duodenum are in their usual locations but are markedly distended, with average diameter of 3.5 cm. The jejunum is also markedly distended and makes three loops, which, together with the stomach and duodenum, occupy at least 75 per cent of the peritoneal cavity. On tracing the intestinal loops, the jejunum ends in a blind dilated sac about 12 inches from its commencement. The remainder of the small intestine is represented by a narrow fibrous cord coiled on the anterior surface of the dilated jejunum. The terminal six centimeters of the ileum has a very small lumen of about 0.5 cm in diameter. This portion of the bowel has been anastomosed to the dilated jejunum. The stoma of this anastomosis is open but the distal segments contain no air and only a small amount of semisolid grayish-yellow material. The stoma of the anastomosis measures four millimeters in diameter, and the margins are slightly edematous. The cecum and the ascending colon are flattened and are situated medial to the normal position so that they lie in approximately the midline. The remaining portions of the large intestine are also

flattened but the lumen is patent as in the rectum. The remaining viscera are in their usual locations.

"The liver border is 2.5 cm below the costal margin. The diaphragm on the right is at the level of the 4th rib and on the left at the 4th interspace. The thymus is of the expected size.

"Both pleural cavities are free from excess fluid, and their surfaces are smooth and glistening. The pericardial surfaces are smooth and glistening. The heart is of normal size and the ductus arteriosus is open. The endocardial surfaces are everywhere smooth and glistening. The foramen ovale is open but closed by a flap. The various valves are firm, and the leaflets are normal. The myocardium is dark reddish-gray.

"The lungs are similar in general appearance, both being heavy, dark reddish-gray and airless. On section, the lung tissue is bluish and contains many confluent, firm consolidated areas. A moderate amount of frothy, yellowish fluid can be expressed from the upper lobes."

Case 5—Baby B, a white female, was born at Baylor Hospital October 10, 1941. Full term. Normal delivery. Weight Seven pounds, four ounces. Vomiting first occurred when baby was three days old and was intermittent thereafter. Vomitus was bile-stained several times. Visible peristalsis was recorded at times, waves passing from left to right in the upper abdomen. On October 22, 1941 barium was given by mouth, and some delay in emptying of the stomach was noted, but no organic obstruction could be demonstrated. On October 26, 1941, the baby was discharged, having shown some improvement on thickened feedings and atropine. Vomiting had at times been projectile. Stools were normal in appearance and amount.

After leaving the hospital, symptoms became promptly worse. Projectile vomiting after almost every feeding began. A small tumor was thought to have been felt in the region of the pylorus. Weight dropped to six pounds, two ounces.

On October 31, 1941, the baby was readmitted to the hospital. *Clinical Diagnosis* Hypertrophic pyloric stenosis. Saline and glucose given by hypodermoclysis.

Operation—November 1, 1941. Under light ether anesthesia, a short right upper rectus incision was made and later lengthened. The stomach and duodenum were moderately dilated, and, at the pyloric ring, the muscle fibers were moderately thickened, but there was no definite pyloric tumor, small intestine, dilated. Below the duodenojejunal junction, the small intestine was collapsed and cyanotic. The cecum was found in the left upper quadrant of the abdomen, where it was held by a thin fold of peritoneum, which extended across the duodenojejunal ligament to the iliac fossa on the right. The entire small intestine was found to be rotated at its mesenteric attachment through 360° in a counter-clockwise fashion. The sigmoid colon was extremely long, extending into both upper quadrants. In addition to the circulatory obstruction of the small intestine, there was obstruction of the lower portion of the duodenum just above the duodenojejunal junction by the abnormal peritoneal fold, to which the cecum was attached. There was no attachment of the mesentery of the small intestine except at the point of entrance of the superior mesenteric artery (Fig 5).

The stomach was first examined, and the thickening at the pyloric ring incised longitudinally through an incision about one centimeter long. The muscle fibers were separated and the mucosa allowed to bulge through the incision to the level of the serosa. The abnormal peritoneal fold was sectioned, allowing the volvulus to be reduced by clockwise rotation through 360°, and the cecum was then replaced in the right lower quadrant, but no attempt was made to attach it. After reduction, the color of the small intestine became normal and the intestine rapidly filled with gas. The wound was closed in layers without drains, using fine cotton No 100 throughout. *Postoperative Diagnosis* Extrinsic obstruction of the duodenum, incomplete rotation of the cecum, volvulus of the small intestine, early hypertrophic pyloric stenosis.

Postoperative Course Saline and glucose solution given by hypodermoclysis. Nothing was given by mouth for 24 hours, then water in small amounts was started.

and retained Thirty-six hours after operation, a formula of equal parts evaporated milk and water was given in half ounce amounts and mostly retained The amount of the formula was increased gradually to three ounces every three hours, but, on the fifth postoperative day, vomiting of about half of each feeding began Thereafter, the adjustment of feedings continued to present a problem, but, when discharged, November

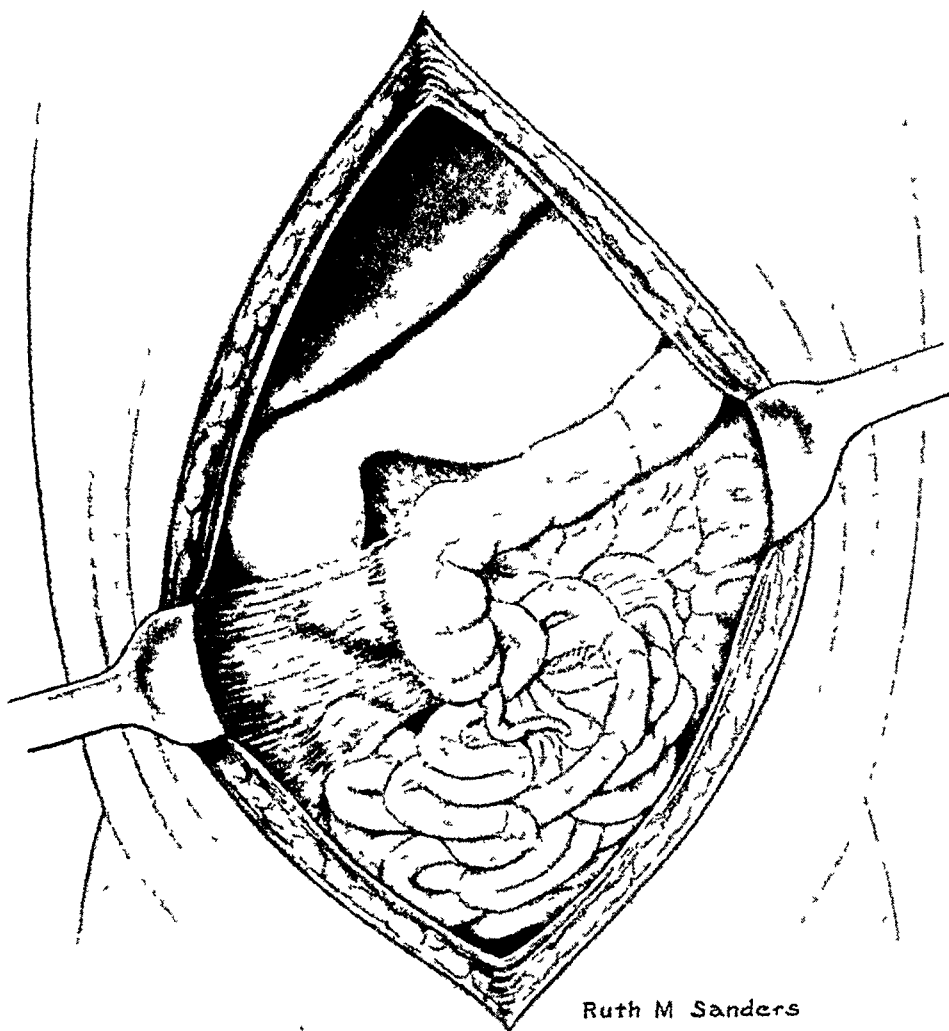


FIG 5 —Case 5 Malrotation of colon, duodenal obstruction by band, volvulus of small intestine

11, 1941, vomiting was occurring only once or twice a day, and there was a steady gain in weight This course continued for the next three weeks, then vomiting ceased and has not recurred Normal development has continued

Case 6 —Baby D a white male, was born at Good Samaritan Hospital December 6, 1941 Full term pregnancy Difficult delivery with high forceps, resulting in two cephal-hematomata When two days old, the baby had a convulsion and began vomiting One small bowel movement of meconium was passed

Admitted to Bradford Memorial Hospital, December 9, 1941, vomiting frequent small amounts of bile-stained fluid and retaining nothing taken by mouth Barium was

given by mouth and roentgenograms showed a greatly dilated stomach and duodenum. No barium passed beyond the duodenum.

Weight. Five pounds, eight ounces. There was moderate dehydration and slight jaundice. A large cephalhematoma was present on each side of the head in the occipitoparietal regions. There was no cyanosis and no sign of increased intracranial pressure. The abdomen was slightly distended, and peristaltic waves passing from left to right across the upper abdomen were noted at times. Examination was otherwise normal. *Clinical Diagnosis.* Duodenal atresia. Saline and glucose solutions and a blood transfusion were given in preparation for operation.

Operation. December 11, 1941. Under light ether anesthesia, a right upper rectus incision was made. The stomach and duodenum were greatly dilated and hypertrophied, and the pyloric ring was identified with difficulty, since the pylorus and duodenum were uniformly dilated to a diameter of about five centimeters. The point of obstruction was at or near the duodenojejunal junction, and was intrinsic. The jejunum and the remaining portions of the small intestine were normal in appearance, but completely collapsed. Cecum, appendix, and ascending colon were also normal. The transverse colon was displaced upward and the transverse mesocolon stretched over the enlarged duodenum (Fig 1).

The dilated stomach and duodenum were collapsed by catheter passed through the mouth and the location of the obstruction was identified. The entire small intestine was examined and found to be normal. An incision was made through the mesocolon at an avascular area, through which the lowermost part of the wall of the duodenum was drawn and attached by an anchoring suture to the proximal portion of the jejunum as close to the duodenojejunal junction as possible. A side-to-side anastomosis was made, using two layers of fine cotton sutures. The stoma was about 25 cm in length. The wound was closed in layers, using fine cotton sutures.

Postoperative Course. Concentrated blood plasma given intravenously immediately after operation. Nothing was given by mouth for 24 hours, then water four cubic centimeters every hour, was started and increased gradually as no vomiting occurred. Forty-eight hours after operation, breast milk was given but part of each feeding was vomited. Vomitus was heavily bile-stained. A regimen of gastric lavage immediately preceding each feeding was begun and vomiting promptly stopped. Normal stools were passed daily after feedings began. Weight gain was slow but increased from five pounds two ounces, before operation to six pounds, thirteen ounces at discharge, January 10, 1942, 30 days after operation. Wound healing was delayed by small areas of subcutaneous suppuration, but, at discharge, there was a firmly healed scar. Development proceeded normally. On February 11, 1942, the baby weighed nine pounds, and was apparently in excellent health.

DISCUSSION.—It is significant that the last five of these six cases were encountered during a period of six months, while the first was operated upon three years earlier. This may be coincidence, but it is more likely explained on the basis of an increased awareness of the occurrence of congenital obstruction in the newborn. It is encouraging to feel that more and more early diagnoses will be made, and that the list of successful operations will grow rapidly larger. We have no original contributions to make either to diagnostic methods or surgical procedure. We have been impressed, however, with the beneficial effect of concentrated blood plasma in the postoperative treatment of our recent cases. When plasma has been given intravenously immediately after operation no signs of shock have occurred and the postoperative course in each case has been astonishingly smooth. Another technical detail of possible interest is the use of very fine cotton thread No. 100, as

the only suture material. Except for a minor skin infection in one case, we have encountered no difficulty in wound healing when fine cotton has been used throughout the operation. It seems particularly adapted for this type of surgery.

REFERENCES

- ¹ Ladd, W. E., and Gross, R. E. Abdominal Surgery of Infancy and Childhood. Philadelphia, W. B. Saunders Co., 1941.
- ² Ladd, W. E. Congenital Duodenal Obstruction. *Surgery*, 1, 878, 1937.
- ³ Miller, E. M. Bowel Obstruction in Newborn. *ANNALS OF SURGERY*, 110, 587, October, 1939.
- ⁴ Cohen, P. Congenital Intestinal Obstruction. *Am Jour Dis of Child* 61, 135, January, 1941.
- ⁵ Glover, D. M., and Hamann, C. G. Intestinal Obstruction in the Newborn Due to Congenital Anomalies. *Ohio State Med Jour*, 36, 833, August, 1940.
- ⁶ Elman, Robert. Ladd's Operation for Cure of Incomplete Rotation and Volvulus of the Small Intestine Producing Duodenal Obstruction in Infancy. *ANNALS OF SURGERY*, 112, 234, August, 1940.
- ⁷ Donovan, Edward J. Congenital Atresia of the Duodenum in the Newborn. *ANNALS OF SURGERY* 103, 455, March, 1936.
- ⁸ Stetten, De Witt. Duodenojejunostomy for Congenital Intrinsic, Total Atresia at the Duodenojejunal Junction. *ANNALS OF SURGERY*, 111, 583, April, 1940.
- ⁹ Lee, Walter Estell. Discussion of Stetten ⁸.
- ¹⁰ Donovan, Edward J. Discussion of Stetten ⁸.

ATRESIA OF THE DUODENUM

CASE REPORT

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THE NUMBER of reported cases of duodenal atresia is small, and the management of such cases fraught with difficulties and disappointments. When infants with this anomaly are encountered, therefore, it is important to record their history in the hope that the addition of some minor detail to the existing knowledge of the condition may aid in the diagnosis and treatment of future patients. We are, therefore, presenting the following case.

Case Report—B. B., a male infant, 30 hours old, was admitted to St. Joseph's Hospital, March 7, 1941. His birth had been uncomplicated. Both parents were living and well, as were seven siblings. One sibling had died of pneumonia in his first year.

When only six hours old the infant vomited a small amount of dark brown fluid. Such vomiting recurred at varying intervals after the ingestion of fluids during the first 24 hours, and caused the physician in charge, Dr. Charles B. Bertolet, to send the child to the hospital. At the time of admission the patient's general condition was good. There was no clinical evidence of dehydration. Examination of the ears, nose, throat, lungs and heart revealed nothing abnormal. The abdomen was soft and not distended. There were no palpable masses. Peristalsis was not audible. The extremities were normally formed and exhibited good tone.

Shortly after admission the patient passed his first tenacious meconium plug. His diet consisted of 5% *Beta*-lactose in one-half ounce portions every four hours, given by a nipple at first, later by gavage. All the fluid ingested was regurgitated as a thick brownish liquid. Elixir of phenobarbital gr. 1/12 and atropine sulfate gr. 1/1,000, given ten minutes before each feeding, failed to prevent the vomiting. Hypodermoclyses of 50 cc. of physiologic saline solution were administered every six hours and Klotogen in 0.5 cc. doses was given every eight hours.

A surgical consultation was held ten hours after the infant arrived at the hospital. At that time the child presented a strange and frightful picture. Streams of fresh blood came from the nostrils and mouth, while the lips and chin were coated with dried blood. Immediately before the consultation the child had vomited two ounces of bright blood. The skin was mildly dehydrated. Pinching the skin elicited a lusty cry. The abdomen was soft but slightly distended. The liver edge was easily palpable, extending from the xiphoid process to the right anterior superior iliac spine. An indefinite tubular structure was palpable extending from the midpoint of the left costal margin downwards towards the umbilicus. Peristaltic waves were not visible.

The diagnoses listed in order of preference were: 1. Duodenal obstruction, either extrinsic or intrinsic; 2. volvulus; and 3. an hemorrhagic diathesis, together with some form of high intestinal obstruction.

On March 8, 1941, 24 hours after admission, a roentgenographic examination was performed. Fluoroscopically, the chest, heart and diaphragm appeared normal. A small amount of barium passed unimpeded down the esophagus, outlined the stomach normally, and then passed through the pylorus. The barium collected in the first portion of the duodenum and had remained there at the time of the second examination 24 hours later.

Roentgenologic Diagnosis Duodenal obstruction.

Operation was performed March 9, 1941, at 4 P.M. Preoperative medication consisted of sodium phenobarbital gr. 1/4 hypodermically at 3:15 P.M. Analgesia was ob-

ATRESIA OF DUODENUM

tained by means of a whiskey sugar-teat, and anesthesia by 1% procaine infiltration. A right rectus muscle-splitting incision was made.

Examination revealed a dilatation of the pylorus to 1.5 cm, and a dilatation of the first portion of the duodenum to 3.0 cm. At the line of juncture with the second portion of the duodenum this dilatation of the first portion ended abruptly in a rounded, blind sac. A hiatus, of about 2 mm in width, separated the first and second portions of the duodenum. The second portion was slightly distended and was tinged green-black by the bile which it contained. Examination of the stomach, jejunum, ileum, and colon revealed no gross abnormalities.

A duodenojejunostomy was effected between the dilated first portion of the duode-



FIG 1—Roentgenogram showing the dilated first portion of the duodenum filled with barium, 24 hours after barium was ingested.

num and a loop of jejunum about 10 cm distal to the ligament of Treitz. The anastomosis was held by means of an outer row of interrupted and an inner row of continuous sutures, posteriorly, and a Connell suture and outer row of interrupted sutures, anteriorly. Arterial silk No 00000 was used throughout.

It was necessary to induce light ether anesthesia to close the abdomen. The peritoneum and rectus sheath were closed as one layer with closely placed interrupted sutures of No 00 silk. Interrupted vertical mattress sutures of No 00 silk approximated the skin edges.

A transfusion of 70 cc of citrated blood was administered immediately after operation. The postoperative reaction was negligible. Aspiration of the stomach contents every four hours, during the first 48 hours, yielded 2 to 8 cc of bile-colored fluid. Sterile water was given in amounts not exceeding 15 drops every two hours, and 50 cc saline infusions were continued, hypodermically, every six hours. Sulfanilamide, 15 cc of 0.8% solution, was added to each infusion.

Twenty-four hours after operation the infant became cyanotic and developed rapid, irregular breathing. Simultaneously, tetanic contractions of the hands occurred. These phenomena were relieved by inhalations of oxygen and intramuscular injections of

calcium gluconate. Physical examination of the lungs revealed no abnormal signs.

On the second day after operation there were several short-lived attacks of respiratory difficulty which were relieved by oxygen inhalations.

On the third day ten drops of 5% glucose solution, alternating with ten drops of mother's milk, were taken every hour. Regurgitation of indeterminate amounts of bile-colored fluid occurred. A dark green stool indicated that bile was passing through the anastomosis. A urine specimen gave a strongly positive reaction for acetone. To combat this acidosis 2.5% glucose solution was added to the saline infusions. A second transfusion of 70 cc of citrated blood was administered. The temperature dropped to 99.8° F at the end of the third day.

On the fourth day a disruption of the central two-thirds of the wound was discovered, with the anterior surface of the right lobe of the liver filling the gap. The skin edges were approximated with strips of adhesive plaster and a vaselined gauze dressing was applied. Resuture was postponed in the hope that improvement in the general condition might occur as the function of the duodenojejunosomy became established. The child was taking 160 cc of milk and glucose solution by mouth in 24 hours, and regurgitating about one-half this intake. The temperature remained normal on the fourth day and until noon of the fifth day postoperatively.

The volume of fluid regurgitated diminished on the sixth day and the infant appeared stronger. Therefore, the wound was resutured under light ether anesthesia. Interrupted through-and-through sutures of No. 38 steel wire, extending from skin to peritoneum, were placed in the abdominal wall. Skin edges were carefully approximated with interrupted sutures of No. 40 steel wire. The operation required 37 minutes.

The infant appeared to be severely shocked immediately following the operation, and after 45 minutes respiration became imperceptible but was restored with the aid of a resuscitator. The improvement thus obtained was short-lived. Repeated resuscitation was necessary until death occurred two hours and 45 minutes after operation, March 15, 1941.

Autopsy—This was performed 20 hours postmortem. The cause of death was lobular pneumonia, involving the lower lobes of both lungs. Microscopic examination showed this process to be in the stage of grey hepatization.

Pathologic Examination—*Gross*. The stomach was long and of the fish-hook type. The duodenal bulb was dilated, and a complete atresia was found 3 cm distal to the pylorus. There was no abnormality of the common bile duct which emptied into the second portion of the duodenum just distal to the line of atresia via a dilated ampulla of Vater.

The duodenojejunal anastomosis was intact and there was no evidence of serosal irritation along the suture line. *Microscopically*, numerous fibroblasts were seen in the inflammatory exudate which cemented the serosal surfaces. This degree of healing appeared to be normal for the elapsed time.

SUMMARY

This is a report of a case of congenital atresia of the duodenum in an infant 30 hours old. Roentgenologic examination proved the atresia to be complete. A duodenojejunosomy was performed 50 hours after birth. The child had attacks of respiratory difficulty which recurred with increasing frequency after the second postoperative day. On the fourth day postoperatively the wound was found disrupted. Liquids taken by mouth were retained in one-half to one-third the ingested amounts and there was evidence that the anastomosis functioned. The wound of the abdominal wall was resutured on the sixth day following the first operation. Three hours later the infant died. Autopsy showed the anastomosis to be intact. Bilateral pneumonia was the cause of death.

MULTIPLE ATRESIA OF THE SMALL INTESTINE

CASE REPORT

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OF THE MANY CAUSES of intestinal obstruction in the newborn, multiple atresia is one of the rarest. The case presented herewith, which showed eight separate and complete points of occlusion of the small intestine was observed at Cleveland City Hospital. From a cursory review of the literature, it seems probable that fewer than 100 such cases have been reported.

Webb and Wangenstein¹ estimated that some form of congenital obstruction of the bowel is found approximately once in 20,000 births. Ladd² reported 60 cases of obstruction due to intestinal anomalies, of these 40 were due to intrinsic defects. Glover and Hamann³ reviewed the records of three large general hospitals in Cleveland, covering a 17-year period, and were able to collect 18 cases of acute intestinal obstruction due to anomalies, of these, five showed points of atresia. Davis and Poynter,⁴ who studied a large series of cases in 1922, believe that in approximately 15 per cent of the atretic cases the points of atresia are multiple.

Case Report—Baby G, white, female, was born August 18, 1940 at 1 00 P M, about two months prematurely. Previous to admission to the hospital the baby was kept at home in a basket, without any form of external heat. On the day after birth, following the mother's attempt to give her some boiled water, she vomited a small amount of bile-stained fluid. Until admission to the hospital, August 20, 1940, almost two full days after birth, she had retained no significant amount of water or milk. There had, furthermore been no stool or passage of meconium.

At the time of admission, physical examination showed a premature, moderately icteric infant, whose temperature was 35°C. Following each feeding she vomited bile-stained fluid, and peristaltic waves passing from left to right could be easily seen in the epigastric region. Several small enemata were given, following which only colorless mucus was passed. Roentgenologic studies, made on the morning following admission, showed the stomach and duodenum to be greatly distended with gas, but no gas was visualized in the remainder of the small intestine or colon (Fig 1). After the administration of a small amount of a barium suspension by mouth, the dilated stomach was readily filled by the contrast medium, as were the first and second parts of the duodenum. The third part of the duodenum (as shown in the oblique views) seemed to lie anterior to and below the stomach, and then appeared to pass about the greater curvature of the stomach to the left and come to a blunt point of occlusion behind the stomach. Beyond this point neither gas nor barium would pass. The interrugal folds of the duodenum were readily visualized (Fig 2).

Combining the history of vomiting bile-stained fluid from the time of the first feeding, the physical evidence of dilatation and visible peristalsis in the stomach, and the roentgenographic evidence of distal duodenal obstruction, with anterior position of the duodenum, the operator (D M G) thought that the evidence favored a diagnosis of unrotated colon with volvulus of the small intestine about the superior mesenteric artery. With this preoperative diagnosis, an exploratory celiotomy was performed, under local anesthesia, through a small upper right transverse incision.

Operative Pathology Upon opening the peritoneum, an enormously distended loop of intestine presented. The stomach and duodenum were markedly distended, with flecks of barium visible through the thinned-out visceral wall. The duodenum, which was about 2 cm in diameter, occupied an anterior position below the stomach, in front of

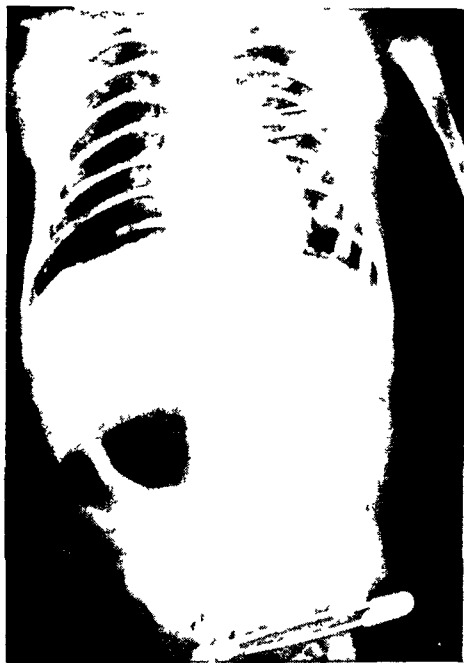


FIG 1—Roentgenogram showing the distended, gas filled stomach and duodenum



FIG 2—Roentgenogram showing stomach and duodenum partly filled with barium and gas. Neither barium nor gas can be seen beyond the distal duodenum, which clearly shows interrugal folds

the superior mesenteric artery, curving to the left behind the stomach and ending blindly at a point, roughly, in the position of the duodenojejunal junction. The cecum and appendix were just to the left of the midline below and behind the duodenum. The distal ileum entered the cecum from right to left, and the entire colon occupied the left side of the abdomen, in unrotated fetal position. The small intestine was collapsed, very small in caliber, and occupied the right lower abdomen. It was impossible, without completely eviscerating the infant, to determine the exact position of the proximal jejunum. A loop of small intestine, which seemed large enough to make an anastomosis possible, but which was actually only about 4 mm in diameter, was anastomosed to the blind end of duodenum, by the end-to-side method, using fine silk sutures throughout, without the use of clamps. Gas and fluid passed immediately into the small intestine from the duodenum. The abdominal wall was closed in layers with fine catgut.

Following operation the infant began taking a small amount of formula every hour, and regurgitated only a little. On the second postoperative day a small, yellow stool was passed. On the third postoperative day (August 23, 1940), however, the infant became weak, cyanotic, and died.

ATRESIA OF INTESTINE

Autopsy—Gross Pathology External examination revealed moderate icterus. There was a healing scar in the right upper quadrant, 4 cm in length. No anomalies of the external surface, head or extremities were noted.

Section revealed the thoracic and abdominal organs, other than the intestinal tract, to be in the usual position. The stomach was slightly distended. The intestinal tract showed complete lack of rotation. The entire duodenum was markedly dilated. The



FIG. 3—The postmortem appearance of the abdominal viscera. The distended duodenum may be seen on the left anastomosed to the ileum. The cecum and appendix are in the midline below the stomach.

first and second portions were in the usual position but the third, instead of passing over the vertebral column in the usual manner, passed downward on the right side of the abdomen and, at the height of the umbilicus, turned cephalad into the epigastrium and crossed the spinal column in its terminal portion to end blindly. A loop of ileum 8 cm from the ileocecal junction had been attached in side-to-end anastomosis to this blind end. The jejunum began in the root of the mesentery as a filamentous strand 1 mm in diameter, gradually widened to an average diameter of 5 to 8 mm, then terminated abruptly in a blind end. In the remaining distal portion of the jejunum and ileum seven additional areas of atresia were found (Figs 3 and 4). The segments of intestine between these atretic areas varied from approximately 2 to 5 cm in length, were

cylindrical, and had bluntly rounded ends. The portions of the mesentery between the segments ended in slightly thickened rounded free edges. The entire root of the mesentery was on the left side of the spine. The final segment of the small intestine measured about 18 cm and emptied into the cecum which was found in the left upper quadrant. The appendix was normal. The colon extended by a free mesenteric attachment in the left colic gutter to the pelvis where it terminated in the sigmoid and rectum in the usual manner. The serosal surfaces in the region of the anastomosis were covered by a light reddish-brown fibrinous exudate. The stoma of the duodeno-ileostomy was very small but patent, and no obstruction in the intestinal tract distal to the anastomosis was found.

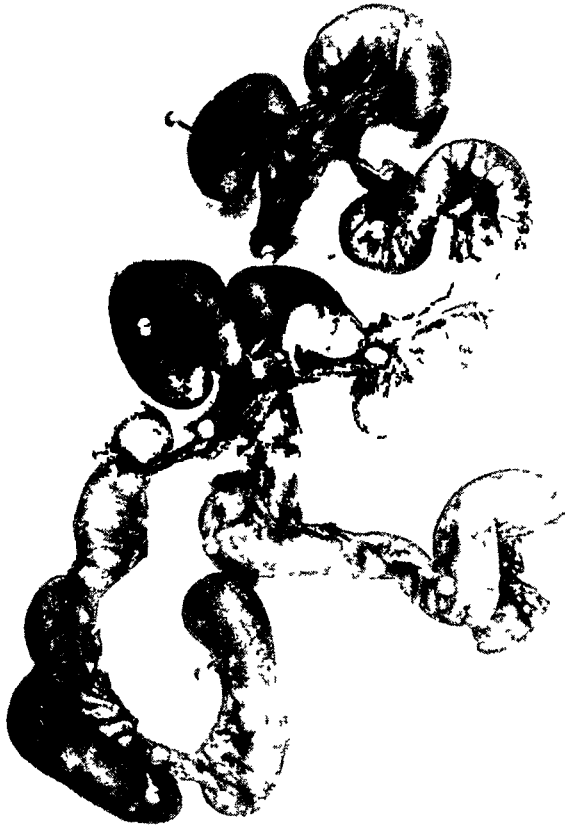


FIG 4.—The postmortem specimen showing seven areas of atresia in the small intestine

Microscopic The segments of the intestine ended in normal mucosa and submucosa. However, as shown by serial sections, both the longitudinal and circular muscle layers of the intestine, diminished in size, continued across the gaps in the mesentery and linked succeeding segments. This muscle showed no microscopic abnormalities other than small size of the layers. Cross-sections of the portions of mesentery between the blind ends of intestine showed muscle fibers, longitudinally and circularly disposed, surrounding a mass of connective tissue either completely or partially, the mesenteric side being composed of loose vascular connective tissue. A section of the duodenojejunostomy showed edema, hyperemia, mild acute inflammation, necrosis, clusters of cocci, and amorphous masses. These changes were more marked in the duodenal than in the ileal wall.

Sections of lungs, liver, spleen and kidneys showed moderate passive hyperemia. A few small focal hemorrhages were seen in the lower lobe of the left lung and in the pyramids of the kidneys.

REFERENCES

- ¹ Webb, C H, and Wangenstein, O D Congenital Atresia of Intestines Am Jour Dis Child, 41, 262-284, 1931
- ² Ladd, W E Congenital Obstruction of the Small Intestine, J A M A, 101, 1453-1458, Surgical Diseases of the Alimentary Tract of Infants New England J, 215, 705, 1936
- ³ Glover, D M, and Hamann, C A Intestinal Obstruction in the Newborn Ohio State Med J, 36, 833-840, 1940
- ⁴ Davis, D L, and Poynter, C W M Congenital Occlusion of the Intestines Report of a Case of Multiple Atresia of the Jejunum Surg, Gynec and Obst, 34, 35, 1922

A LARGE SUBACUTE GASTRIC ULCER

CASE REPORT

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MOST GASTRIC ULCERS seen in reported autopsy and surgical material are chronic or of the acute perforating variety and conform to the usually described round or ovoid ulcer of Cruveilhier^{1, 2}. Descriptions and illustrations of gastrosopic studies⁴ made during the progress and development of gastric ulcers do not alter this general impression.

The following is reported chiefly to illustrate the unusual form of a large subacute ulcer, surgically removed because of hemorrhage and obstruction, thought to be due to gastric malignancy. The pattern of the ulcer bed and its apparent coincidence with the distribution of the subserosal blood vessels of the lesser curvature of the stomach is likewise considered noteworthy.

Case Report—E D, Negro, male, age 51, was admitted to the Station Hospital, Camp Lee, Va, November 10, 1941, with the chief complaint of vomiting "coffee ground" material. Prior to admission, October 31, 1941, he had first complained of loss of appetite and "growling" in his stomach. He had taken three compound cathartic pills and had had three copious bowel movements containing mucus but no gross blood. He was unrelieved of the cramping pain but the catharsis and the anorexia persisted. On November 2, he vomited three or four times. During the next week he was unable to retain solid food but could take liquids. Severe cramping pains coming in waves, preceded the vomiting. He had not had a bowel movement since November 1, although he had passed flatus. His past history revealed normal bowel function until October 31, 1941. He had had malaria in childhood. Operations had included the excision of a lipoma in 1929 and 1931, and the excision of a fistula in ano in 1931. He was unmarried, denied venereal infection, used alcohol moderately and smoked 10 to 12 cigarettes daily.

Physical Examination—The patient was a well-nourished male, height 71 inches, weight 210 pounds. He was acutely ill. Positive findings were moderate pallor of mucous membranes of the mouth and lips, and slight midepigastic tenderness, but no rigidity. No abdominal masses, tympanites nor increased intestinal activity were noted. There were a few small, shotty inguinal lymph nodes. His heart and lungs were negative. Blood pressure 124/70 mm. Reflexes normal.

Laboratory Data—R B C 5,135,000-4,600,000 W B C 21,000-12,000. The high initial counts were undoubtedly due to dehydration. Hb, 95-80 per cent (Tallqvist). The blood Kahn was positive on November 17, and again on November 27, 1941. Gastric Analysis—November 12, 1941. Total acidity of 75 units, and a free hydrochloric acid of 45 units. Pus cells and R B C were abundant. Roentgenologic examination, November 13, 1941, revealed an "ulcer niche of the stomach on the superior margin of the pyloric area with evidence of infiltration which is strongly suspicious of malignancy." **Preoperative Clinical Diagnosis**—Carcinoma of the stomach with obstruction.

Preoperative Course and Management—General supportive treatment was instituted, including gastric drainage by the method of Wangensteen, and water electrolyte balance was controlled by the intravenous route. During this period there was considerable gastric distress and the drainage continued to contain blood. The patient steadily lost in strength and weight, as it was impossible to pass the duodenal tube beyond the pylorus and into the duodenum for feeding purposes, due to the apparent obstruction. He had two blood transfusions of 500 cc of whole citrated blood. Early nutritional edema developed on or about November 17th, so that it was decided that surgical intervention was necessary despite the inability to improve his nutrition.

Operation (J B M)—November 19, 1941. Under general anesthesia (gas induction open drop-ether), a large ulcer-bearing area of the pyloric region was found, with greatest tumefaction and hyperemia at the lesser curvature and extending almost to the greater curvature on both gastric walls. There were no adhesions or enlargement of the regional or mesenteric lymph nodes, neither did exploration reveal nodules of the liver or retroperitoneum. A subtotal resection was accomplished by removing between one-third and one-half of the stomach. Intestinal continuity was reestablished by the anterior Polya method. A Witzel-type jejunostomy for feeding purposes was established in the proximal loop of the jejunum about four inches below the anastomosis. The catheter was threaded through the mesentery and brought through a separate stab incision to the left of the exploration incision, which was an upper left rectus type. One of us (J B M) has for a number of years adopted this procedure as a part of the operative technic for postoperative feeding,⁵ with substantial benefit to all patients so treated.

Postoperative Course—The postoperative course was exceedingly smooth. Of especial interest was the feeding problem which was made simple by the jejunostomy. For a number of years the formula of Scott and Ivy⁶ had been used with benefit, but in this instance the simplified formula recommended by Clute and Bell⁷ was found to be entirely adequate, and in a military hospital has much to recommend it because of the simplicity of preparation. The hydration and nutrition of the patient immediately improved, and by the fourth postoperative day he stated that he felt strong enough to get out of bed. The jejunal feedings were continued for a week (about 2500 calories per day, with adequate protein, fat, carbohydrate, electrolyte and vitamins being given each 24 hours by a feeding schedule which continued through the day, save from 10 P M to 4 A M). The apparatus used was one previously described,⁵ and consists of a narrow blood burette with a controlled Murphy drip in the system to the catheter. Too rapid flow caused increased peristalsis with pain and diarrhea (about one hour was allowed to introduce the 250 cc feeding to the jejunum). The formula of Clute and Bell has the further advantage that it is low in fat. The tendency to diarrhea noted in other feeding formulas was absent. Supplemental feedings by mouth were instituted after the first week, and on the twelfth postoperative day the jejunal tube was removed.

A gastric analysis, December 10, 1941, revealed a total acidity of 15 units, but no free hydrochloric acid. Antiluetic therapy was also instituted at this time.

A generous diet was ordered and he had regained his strength by December 15, 1941, when he was discharged.

Pathologic Examination—*Gross*—The truncated horn-shaped specimen consisted of the amputated distal portion of the stomach, and measured eight centimeters along the lesser curvature and 12 cm along the greater curvature. The diameter of the fundus portion was seven centimeters, while that of the pyloric end was four centimeters. The amputation margins had been crushed. The peritoneal surface was moderately hyperemic and there were numerous petechial hemorrhages in the edematous fatty mesentery of the lesser curvature. Many catgut ligatures were present on the curvatures. When spread out, the excised portion measured roughly 16 x 10 cm. There was an extensive saddle- or girdle-like ulceration centered at the lesser curvature, three centimeters from the

FIG 1



(A)



(B)

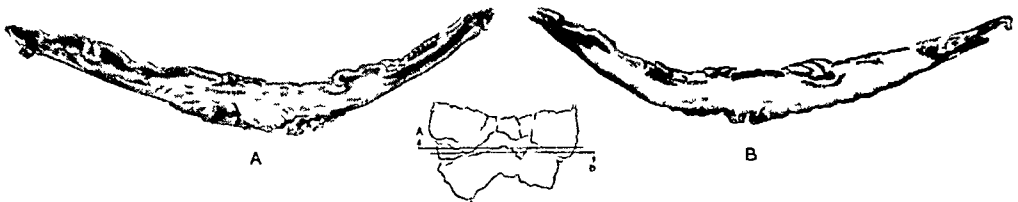


FIG 2

FIG 1—(A) Drawing of pyloric portion of resected stomach including the ulcer. The shape and extent of the ulcer pattern in comparison with the vascular distribution on the serosal surface (B) is noteworthy. The prominence of the eroded blood vessels is exaggerated in the drawing. FIGURE 2 shows the gross characteristics of longitudinal sections of the two edges of the ulcer. (Drawings by Pvt Raphael Epstein, Med Dept U S Army.)

pyloric amputation level, extending circumferentially four centimeters along the anterior and 4.5 cm along the posterior wall. It tapered from 1.5 cm in its widest portion at the lesser curvature to narrow grooves extending to within two centimeters of the greater curvature on both walls. The margins of the ulceration were rolled and smooth. There was considerable edema and hyperemia including petechial hemorrhages in a region two to three centimeters on either side of the ulceration at the lesser curvature. There was little induration. The flat ulcer floor was eight millimeters below the mucosal margins. The surface was granular with fibrin, clotted blood and glairy mucous, which was readily wiped off. In the wide portion of the ulcer two blood vessel stumps protruded about 0.5 mm above the ulcer bed. These had an outside diameter of one millimeter. The lumens contained clotted blood (Figs 1 and 2).

Microscopic—The mucosa at some distance from the margin of the ulcer was composed of slightly hypertrophic glands between which were scattered moderate numbers of plasma cells. A few solitary lymphoid follicles lying in the deeper parts of the mucosa were considerably enlarged and had conspicuous reaction centers. At the margin of the ulcer, the mucosa, rather abruptly, became thinner, the glandular structures were lost until, at the very edge of the ulcer, a single layer of epithelial cells formed the sole remnant of the mucosa.

The surface of the ulcerated area consisted of clotted plasma in which lay degenerating leukocytes and cell detritus. The entire gastric wall beneath the ulcer, as well as beneath the still preserved mucosa, was edematous and everywhere infiltrated by leukocytes, lymphocytes, plasma cells and histiocytes. The muscle had been replaced, in some areas, by granulation tissue, composed of newly-formed capillaries and fibroblasts in various stages of maturity. Here and there, but particularly in the deeper portions of the wall, was an abundant fatty areolar tissue. In the deeper parts there are also numerous nerve bundles and small nerve ganglia, most of which were imbedded in the inflammatory reaction which extends to the serosa.

In a section from a portion near the ulcer, the surface was covered with gastric mucosa which in one region was thickened to nearly twice normal. This region was sharply delineated and consisted of normally arranged, slightly hypertrophic glandular tissue, with much lymphoid hyperplasia. The submucosa contained fatty-areolar tissue and presented inflammatory reaction similar to that described above. There were a few small hemorrhages. In none of the sections was there any evidence of malignancy. There was no indication from a study of the blood vessels, of vascular alteration of syphilitic or sclerotic nature. Preparations from the ulcer margins of the unfixed fresh tissues examined by darkfield illumination failed to reveal spirochaetal forms. *Pathologic Diagnosis*—Subacute ulcer of the stomach with marked inflammatory reaction (Figs 3 and 4).

COMMENT—This large subacute gastric ulcer of unusual shape presents several interesting features from a pathologic as well as clinical viewpoint.

The lack of specific alterations of the vascular tissues, the absence of patchy scarring, the failure to find spirochetes in the ulcer margins, and the high gastric acidity unusual in reported gastric syphilis,⁸ would seem to eliminate syphilis as a causative factor in spite of the positive Kahn reaction.

Numerous writers have been concerned with the relationship of the vascular supply of the lesser curvature with the coincidence of ulcer.⁹ Whether this relationship is significant in the case here reported cannot certainly be ascertained, but the conformity of the lesion to the subserosal vascular pattern of the lesser curvature seems especially noteworthy (Figs 1 and 2).

The treatment was obviously surgical to rule out malignancy. The

operation was performed while the nutrition of the patient was impaired by inability to pass a feeding tube beyond the site of obstruction. Operation revealed that this failure to pass the duodenal tube was due to the severity of pyloric spasm.

FIG 3

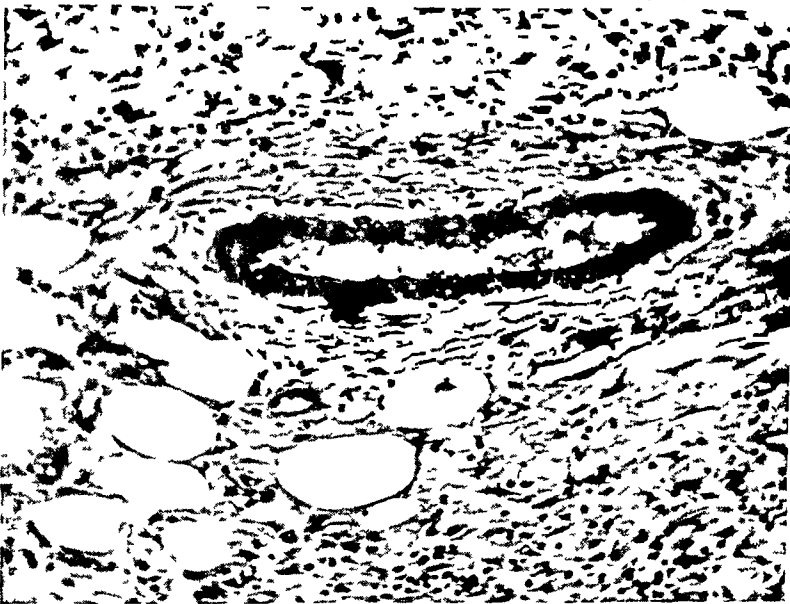


FIG 4

FIG 3—Photomicrograph including a margin of the ulcer. Note the narrow layer of epithelial cells extending to the ulcer floor.

FIG 4—Photomicrograph of a section in the ulcer floor including small blood vessel, without unusual change. Note cellular distribution.

The treatment by medical means might have been attempted but for the two just mentioned reasons. One may speculate as to the subsequent course of this lesion, and its ultimate status—whether complete healing without scarring might occur, or, the far greater likelihood, that had time inter-

vened, that a chronic type of circumscribed indurated ulcer would have eventuated. Thus does one wonder that here, due to impairment of a vascular area, does not necrosis of tissue occur, with loss of tissue substance in the mucosal area so supplied, with reaction and healing of a portion save that where too great a mucosal loss has occurred, and here, due to high gastric acids plus aging of repair, a chronic ulcer of the lesser curvature might not have occurred.

The end-result was satisfactory, in that the man was doing light work two months after discharge from the hospital.

REFERENCES

- ¹ Robertson, H. E. In Eusterman and Balfour. The Stomach and Duodenum. W. B. Saunders Co., 1935, p. 97.
- ² McCarty, W. C. *Ibid*, p. 78.
- ³ Cecil, R. L. A Textbook of Medicine. Ed. 5, W. B. Saunders Co., 1941.
- ⁴ Schindler, R. Gastroscopy. The Endoscopic Study of Gastric Pathology. University Chicago Press, 1937.
- ⁵ Mason, James B. Jejunal Feedings following Operations on the Stomach and Duodenum. Penna. Med. Jour., 41, 1083-1086, September, 1938.
- ⁶ Scott, H. G., and Ivy, A. C. Jejunal Alimentation. An Experimental Study in Dogs. ANNALS OF SURGERY, 93, 1197-1201, June, 1931.
- ⁷ Clute, H. M., and Bell, L. M. Jejunostomy for Postoperative Feeding. ANNALS OF SURGERY, 114, 462-471, September, 1941.
- ⁸ Williams, C., and Kimmelstiel, P. Syphilis of the Stomach, J. A. M. A., 115, 578-582, August 24, 1940.
- ⁹ Reeves, T. B. Studies of Arteries Supplying the Stomach and Duodenum and their Relation to Ulcer. Surg., Gynec. and Obst., 30, 374-385, 1920.

MULTIPLE, PRIMARY NONSPECIFIC JEJUNAL ULCERS, WITH CHRONIC DUODENAL DILATATION

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PRIMARY nonspecific jejunal ulcer and chronic duodenal ileus are both rather rare, but important lesions. In the present instance the chronic duodenal ileus was a complication of jejunal ulcer.

Case Report—N, white, male, age 59, was admitted to Providence Hospital, December 11, 1940, with the history that he had, during the last ten years, passed "black stools" on numerous occasions and had occasional spells of "indigestion and dyspepsia," for which he never consulted a physician. The past history is otherwise irrelevant.

For six months he had vomited one to two hours following meals. At first the vomiting occurred at infrequent intervals and was not in large amounts but grew progressively worse, occurred more frequently, in larger amounts, and was often of greenish color. For several months he has vomited after each meal and even between meals. He has had no epigastric pain nor distress other than a feeling of fullness, which has always been relieved by vomiting.

During the last six months he had lost over 40 pounds in weight, became considerably weakened, and was always moderately constipated. On physical examination he was well-developed but undernourished and dehydrated. His tongue was dry and coated. There was a soft mitral systolic murmur over the apex of the heart and some moist rales at the bases of both lungs. The abdomen was soft, moderately distended and tympanitic. There were no masses or areas of tenderness. Blood pressure 120/60, temperature, pulse and respirations normal.

Laboratory Data R B C 5,160,000, hemoglobin 11.2 per cent, W B C 8,000, with neutrophils 78 per cent, lymphocytes 18 per cent and monocytes 4 per cent. Urine Trace of albumin, and 20 to 25 leukocytes per high power field. Roentgenologic examination demonstrated an obstruction of the small bowel in the region of the ligament of Treitz (Fig 1A). This produced almost complete obstruction, with a marked dilatation of the entire duodenum and stomach. One week later there was still a minimum amount of barium in the stomach, indicating marked gastric delay (Fig 1B). A barium enema showed no abnormalities. **Clinical Diagnosis** Chronic duodenal ileus due to obstruction near the duodenojejunal angle. The obstruction was thought to be an annular carcinoma or ulcer.

He was prepared for operation from December 11 to December 20, 1940. Wangensteen suction drainage was instituted to decompress the stomach and duodenum. Fluid was administered parenterally as 1000 cc. of 10 per cent glucose in saline every six hours, and a liquid diet was given. On the day before operation, he received CO₂ inhalations, digalin intramuscularly and three 5 mg. doses of cortate. Whole blood chloride on this day was 483 mg. per cent, and nonprotein nitrogen 25.9 mg. per cent.

Operation—December 20, 1940. Under continuous spinal anesthesia, the abdomen was opened through a midline incision. The stomach and first part of the duodenum were quite dilated. The jejunum, about one inch below the ligament of Treitz, was markedly adherent to the root of the mesentery in the region of the superior mesenteric vessels and, at this point, seemed to be completely constricted. The jejunum above this point was dilated and the wall thick and edematous. The lymph nodes in the adjacent mesentery were markedly enlarged. One removed for biopsy, proved to be inflammatory.

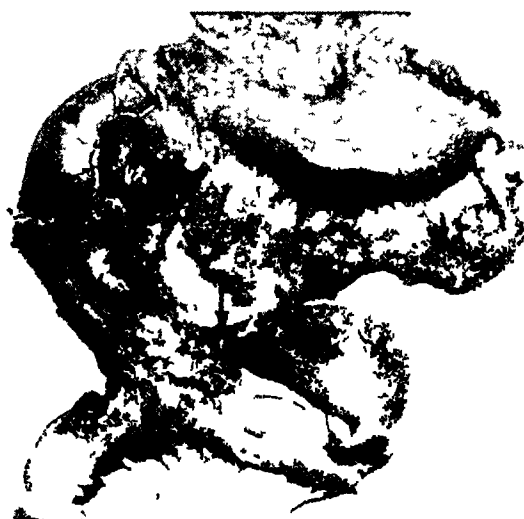


(A)



(B)

FIG 1—(A) Note dilatation of entire duodenum secondary to obstruction near the ligament of Treitz (B) Plain film of abdomen one week after barium meal, showing barium still present, indicating the completeness of the obstruction



(A)



(B)

FIG 2—(A) The stomach and duodenum are dilated but not so markedly as at the time of operation. An arrow indicates the point of stricture (B) Arrow 1 indicates the annular, and arrow 2 the circular ulcer. It was the former which produced the constriction

To accomplish a short-circuiting operation, it was necessary to divide the ligament of Treitz. This allowed mobilization of almost three inches of jejunum and duodenum. A lateral duodenojejunostomy around the obstruction was easily accomplished. Silk was used for the outer layer. Three finger tips could be inserted into the stoma. At the end of the operation the patient began to strain, vomited considerable bile, and became very cyanotic.

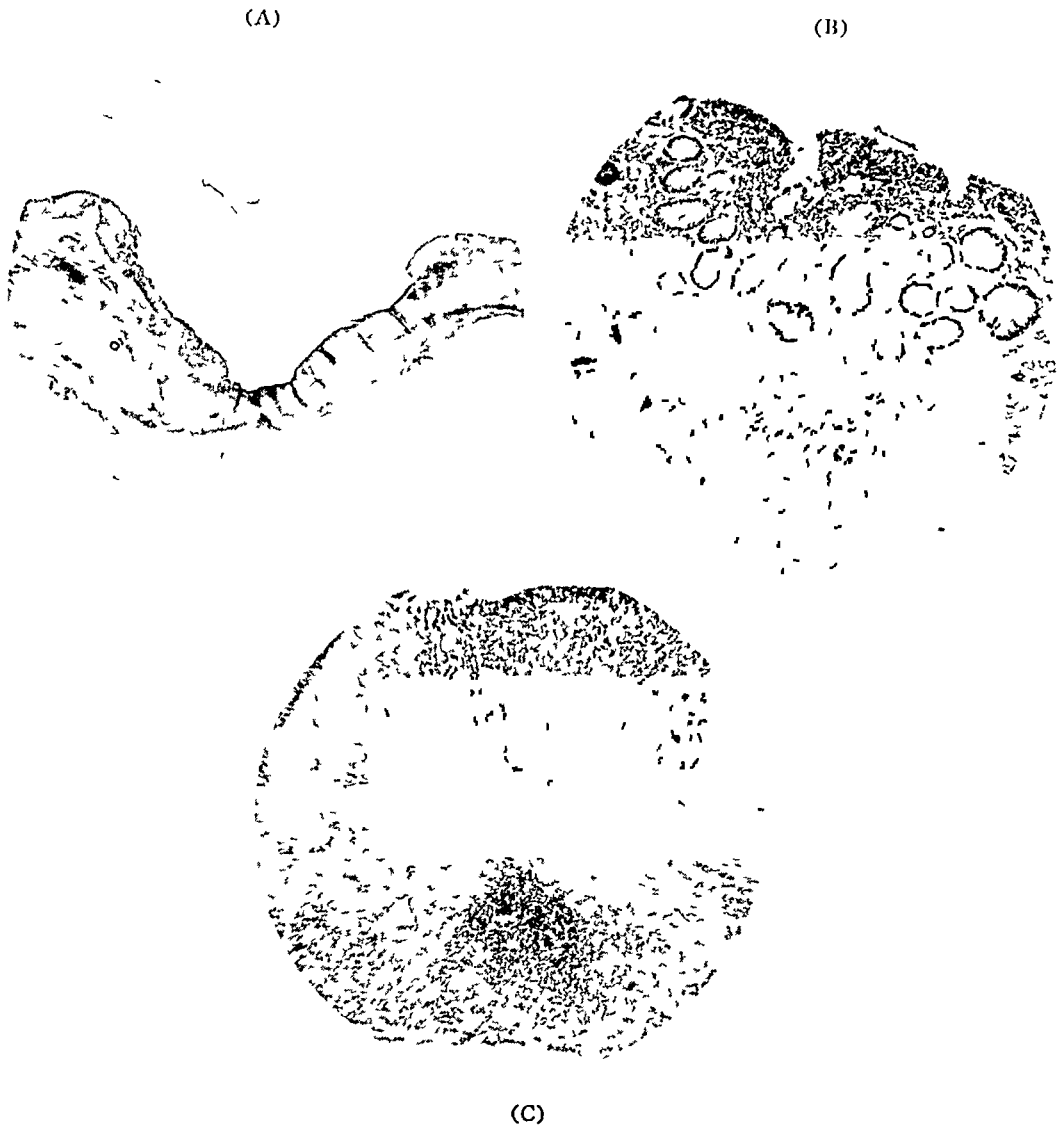


FIG 3—(A) Microscopic sections through the ulcer area—whole section through ulcer (Fig 2)
(B) The border of the ulcer (C) The ulcer base

Postoperative Course—Within 24 hours following the operation the temperature was 106°F, pulse 134, and respirations 24. He was coughing considerably, was very cyanotic and restless. He was placed in an oxygen tent immediately and this was continued up to the time of his death. Whenever it was necessary to continue the oxygen tent he became cyanotic and restless.

On the second postoperative day there was roentgenographic evidence of bronchopneumonia involving the right perihilar region and base of the right upper lobe. From this time on his temperature ranged from 103° to 105°F, the pulse averaged 130, and the respirations 30 per minute. He gradually grew weaker and expired the eighth postoperative day. At no time post-operatively was there any abdominal distention or pain.

Necropsy—The stomach was slightly dilated, and the walls were thick and edematous. The duodenum was markedly dilated and, at a point approximately 3 cm above the ligament of Treitz, there was a duodenojejunostomy. The stoma was of sufficient size and was apparently functioning well. There was no evidence of rupture or perforation at this site (Fig 2A). Immediately distal to the stoma there was a shallow ulcer 1 cm in diameter and approximately 1 cm distal to this there was a completely annular ulcer, which was shallow and had thinned the jejunum at this site (Fig 2B). The circumference of the jejunum at the ulcer was only 2.5 cm. The base and border of the ulcer was thick and fibrous. The pancreas, spleen, liver, and the remainder of the intestine were essentially normal.

Pathologic Examination—Microscopic The stomach wall was thickened and edematous and the mucosa normal. In the jejunum there were a number of changes of considerable importance (Fig 3). In the ulcer-bearing area, the wall was quite fibrous, and throughout the entire portion there was marked infiltration with lymphocytes, most of which were in definite collections. In this area, the plexus of Meissner as well as the ganglion fibers were distinctly swollen and edematous. The mucosal portion was distinctly hyperplastic and contained numerous mitotic figures. The area of hyperplasia merged imperceptibly with an area in which the epithelium was denuded and formed a definite ulcer. At this point there was a distinct penetration of the process into the muscular wall. The base was composed of dense fibrous connective tissue with numerous lymphocytes. There was some fibroblastic proliferation as evidenced by the attempt at repair. The glandular elements in the areas immediately adjacent to the ulcer were dilated and cystic. In the sections examined there was no evidence of heterotopic gastric mucosa.

Discussion—In 1921, Judd³ stated that not a single primary jejunal ulcer had been observed at the Mayo Clinic up to that time. Richardson⁶ (1922) reported the first case in this country. Robinson and Wise⁸ stated that only 13 cases of jejunal ulcer had been reported up to 1940, and most of these were from the European literature. They also stated that "in none of the case reports was a definite diagnosis made before operation." Ebeling¹ (1933) reported his case as the first on record to be diagnosed clinically, as the 42nd case reported in the literature, and the seventh case to be operated upon before perforation. Of the 42 cases, 35 were of the perforating variety and of these, 22 came to operation.

The etiology of primary nonspecific jejunal ulcer is as obscure as is that of the more common duodenal, pyloric, or gastric ulcer. When classified as nonspecific, it is significant that they are not due to any of the known etiologic agents, such as typhoid, dysentery, tuberculosis, syphilis, gastroenterostomy, trauma or tumors. The various theories as to the cause of these ulcers include focal infection, vascular obstruction and thrombosis and hyperacidity from adjacent heterotopic gastric mucosa.

Most of the ulcers, in the cases reported, occurred in the proximal jejunum opposite the mesenteric attachment. With ulcer formation, stenosis occurs as a result of the connective tissue formed in and around the ulcer. Both macroscopically and microscopically the description is similar to that of chronic peptic ulcer. There are very few instances recorded of enlarged lymph nodes. Multiple ulcers were observed in nine of the cases reported.

These ulcers occur most frequently after the age of 20, the majority in middle life. They are twice as common in males as in females.

The typical patient is a middle-aged male, who has a history of mild gastric distress particularly pain in the epigastrium. This may simulate very closely the symptoms of gastric and duodenal ulcers, and with stenosis at the ulcer, there may be pain, distention and vomiting from obstruction. Melena may occur. The patient may have had no previous digestive complaints, but with perforation his symptoms will be similar to those of perforating gastric and duodenal ulcers.

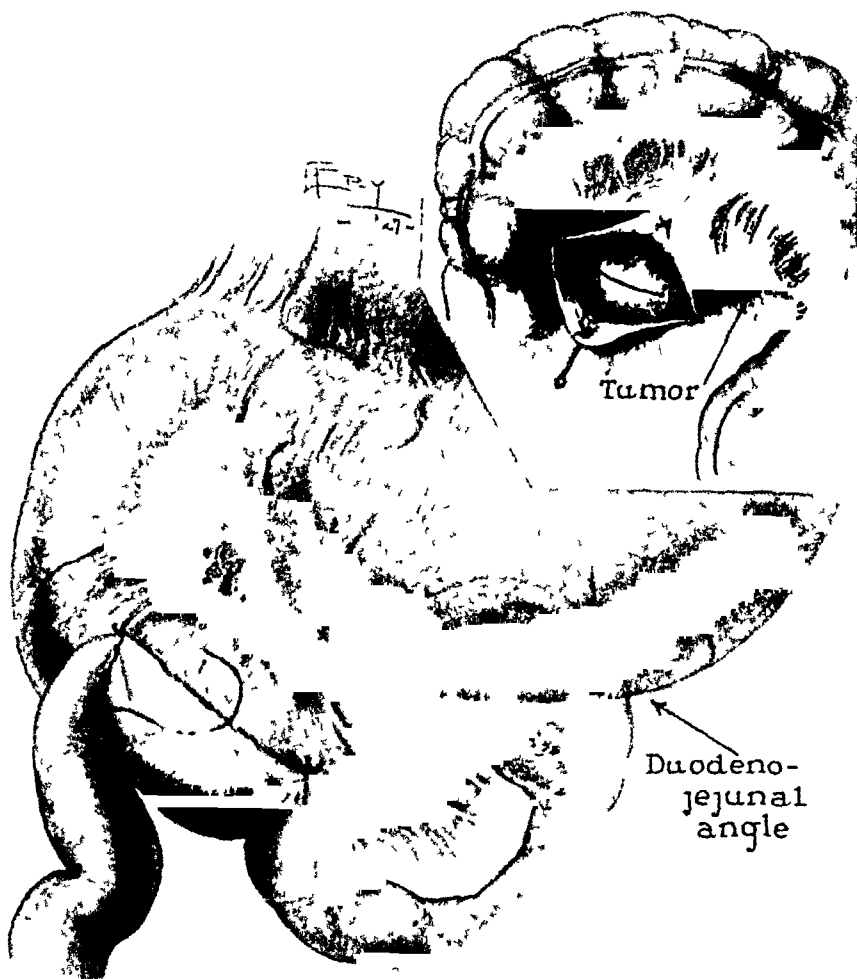


FIG 4.—Drawing of proposed anastomotic method in obstructions near ligament of Treitz (After Eusterman and Balfour-)

Clinically, the presence of simple nonspecific jejunal ulcer is hard to detect, as evidenced by the fact that only one was diagnosed up to 1934. Duodenal ileus should lead one to think of jejunal ulcer. Roentgenologic studies are invaluable in demonstrating these points.

Immediate operative repair is essential for the perforating ulcers. In the nonperforating types, either resection of the ulcer-bearing area or duodenojejunostomy may be performed. The usual duodenojejunostomy is

placed between the jejunum distal to the obstruction and the retroperitoneal duodenum to the right of the mesenteric vessels (Fig 4)

In the present instance, the ligament of Treitz was cut and the duodenum was mobilized for a distance of about three inches above the point of obstruction, and was thus made available for anastomosis with the jejunum

Dilatation of the duodenum, which was such an important factor in this patient, has been classified by Eusterman and Balfour² as follows. Chronic dilatation of the duodenum and chronic duodenal obstruction with dilatation. In the latter group the obstruction may be due to either intrinsic or extrinsic causes in relation to the bowel lumen

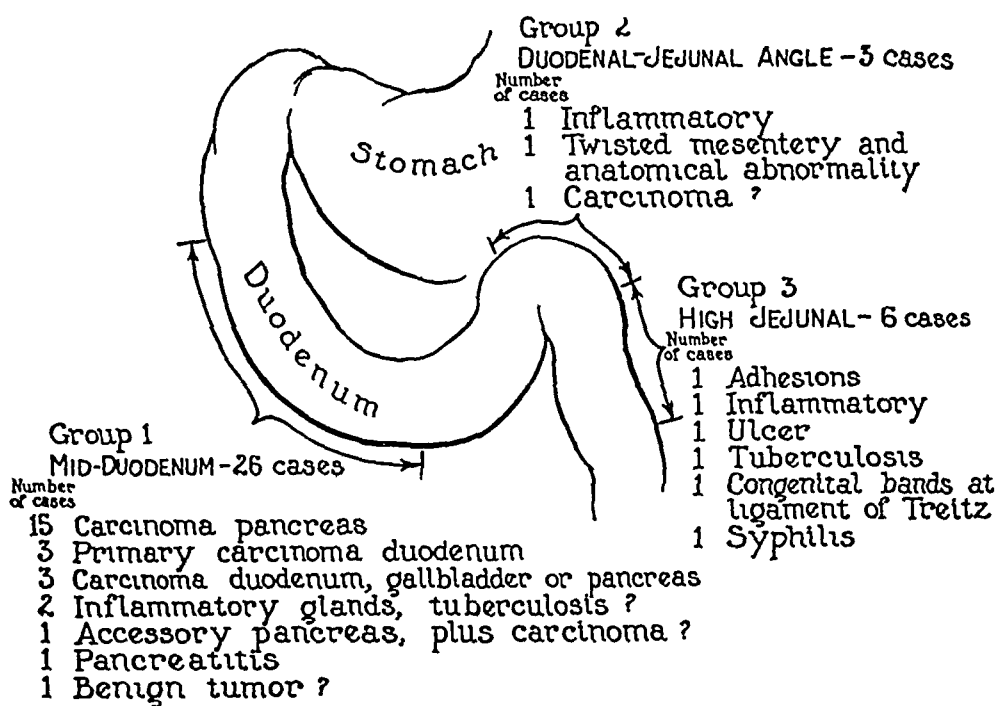


FIG 5—Causes of chronic duodenal obstruction with dilatation (After Rivers and Thiessen⁷)

Among the intrinsic causes of duodenal obstruction are included the lesions of the duodenal wall producing stenosis and lesions or foreign bodies obstructing the lumen of the bowel from within. Among the extrinsic causes are included congenital anomalies and postoperative or inflammatory adhesions.

Rivers and Thiessen⁷ reported 35 instances of chronic duodenal obstruction with dilatation, which were divided into three groups (Fig 5)

In the intrinsic congenital types, septums within the bowel are the usual cause.

Of the intrinsic acquired causes of obstruction, carcinoma, lues, tuberculosis, jejunal ulcer, foreign bodies, gallstones, hairballs, and benign tumors are given as the causes.

The extrinsic types are much more frequent than the intrinsic, and the following are examples of this type. Congenital anomalies resulting in faulty rotation of the intestines, adhesive bands and membranes, postoperative adhesions and bands, extensive adhesions from chronic cholecystitis, growths

and tumors of neighboring organs and lymph nodes, and retroperitoneal new growths

The diagnosis of chronic duodenal dilatation can not be made without roentgenologic examination. Krass and Beck⁴ in an article on chronic duodenal ileus, stated that the diagnosis is exceedingly rare

SUMMARY

The case report of a male, age 59, who had chronic dilatation of the duodenum produced by obstructive multiple jejunal ulcers, is presented. As a means of relief, a duodenojejunostomy was performed, in which the duodenum was mobilized by dissection after dividing the ligament of Treitz.

A brief review of pertinent factors pertaining to primary jejunal ulcer as well as duodenal dilatation due to obstruction is included.

BIBLIOGRAPHY

- ¹ Ebeling, Walter W. Primary Jejunal Ulcer. *ANNALS OF SURGERY*, 47, 857-874, June, 1933.
- ² Eusterman, G. B., and Balfour, D. C. *The Stomach and Duodenum*. Philadelphia and London, W. B. Saunders Company, 1936, 382 pp.
- ³ Judd, E. S. Jejunal Ulcer. *Surg., Gynec. & Obst.*, 33, 120-126, August, 1921.
- ⁴ Krass, E., and Beck, W. C. Chronic Duodenal Ileus. *ANNALS OF SURGERY*, 99, 311-331, February, 1934.
- ⁵ Lahey, Frank H., and Marshall, Samuel F. Some Unusual Gastro-enterological Problems. *Am. J. Dig. Dis.*, 6, 654-664, November, 1939.
- ⁶ Richardson, E. P. Jejunal Ulcer without Previous Gastro-enterostomy. *Surg., Gynec. & Obst.*, 35, 1-10, July, 1922.
- ⁷ Rivers, A. B., and Thiessen, N. W. L. Obstruction of the Upper Portion of the Small Intestine. A Clinical Study. *Am. J. Dig. Dis.*, 1, 92-96, April, 1934.
- ⁸ Robinson, Walter D., and Wise. Simple Nonspecific Ulcers of the Jejunum-Ileum. *Surg., Gynec. & Obst.*, 70, 1097-1099, June, 1940.

MYO-EPITHELIAL HAMARTOMA OF THE ILEUM WITH INTUSSUSCEPTION

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THE PURPOSE of this communication is to present an instance of an unusual benign tumor-like formation of developmental origin, composed of duct-forming epithelium and smooth muscle, occurring in the wall of the ileum of an infant, associated with intussusception, and to discuss briefly the general histologic structure, the classification, and the theories of origin of such a tumor

The frequent association of tumors of the small intestine with intussusception is well recognized. Hence no further comment will be made on this association.

Benign tumors of supposedly developmental origin, composed of epithelium and smooth muscle in varying proportions and degrees of structural differentiation, such as aberrant, heterotopic, or incompletely differentiated accessory pancreatic tissue and adenomyomata, occurring in the gastro-enteric tract, are being reported in increasing numbers. However, until recently there were relatively few references in the literature to such tumors of the small intestine, with or without intussusception. In addition to numerous reports of polypoid adenoma, various other types of benign tumors of the small intestine have been reported, such as fibro-adenoma, leiomyoma, lipoma, fibroma, fibromyxoma, xanthoma, cystadenoma, hemangioma, lymphangioma, endometrioma, and dermoids.

King,¹ in 1917, in a review of 119 collected cases of benign tumors of the small intestine reported up to that time, did not mention the type to be described, nor did Willis,² Raiford,³ Moore and Schmeisser,⁴ Cave,⁵ Joyce,⁶ Fiske,⁷ Goldberg,⁸ or Cohn, Landy, and Richter.⁹ Rankin and Newell,¹⁰ in reporting 24 cases of benign tumor of the small intestine, described one case in which three adenomyomata were grouped together, causing partial obstruction. Clarke¹¹ has recently stated that tumor masses composed of smooth muscle and epithelium are occasionally encountered in the gastro-enteric tract and reported eight such cases along with pertinent references. He classified these tumors as hamartomata, using Albrecht's¹² term, with the additional descriptively qualifying term of "myo-epithelial" to indicate the type of tissue components.

Case Report—Roper Hospital, No 111,679. The patient, Negro, male, age nine months, was admitted to the hospital, July 23, 1940, suffering from constipation and

fever Two days previously the infant had had its last bowel movement, which was said to have contained a few streaks of blood On that day the infant vomited several times and was noted to be very fretful, the mother thought it also had abdominal pains because of frequent crying The apparent pain persisted up until the time of admission The following day the infant vomited four times and began to pass blood from the rectum Thereafter there were frequent passages of blood There was no history of any similar previous attack As far as was known, the infant had been in good health since birth, without any previous serious illnesses

Physical Examination—Temperature 103°F, pulse 126, respirations, 28 The patient was a fairly well-nourished and well-developed Negro male baby who appeared acutely ill There was no cyanosis or jaundice The skin, lips, and tongue were dry The mucous membranes were of good color The heart and lungs were normal The abdomen was diffusely distended, symmetrical and soft throughout Over the upper abdomen there were visible patterns of distended loops of bowel No mass was felt The liver, spleen and kidneys were not palpable There was no hernia On continued observation, the abdominal wall intermittently became rigid, during which time the infant appeared to have abdominal pain On rectal examination, no mass was palpable After withdrawal of the examining finger, there was a bloody discharge from the rectum The remainder of the physical examination was noncontributory

W B C 9,000 Hb 8 Gm Blood Wassermann and Kline negative A specimen of urine was not obtained Prior to operation a plain roentgenogram of the abdomen with the patient in the upright position showed moderate distention of the small intestine with numerous fluid levels present Culture of the peritoneal fluid obtained at operation showed no growth

The diagnosis of intussusception was made, and operation was performed immediately following the administration of parenteral fluids

Operation—Under drop-ether anesthesia, a right rectus, muscle-splitting incision was made On incising the peritoneum, a small amount of clear, odorless yellow fluid escaped A specimen for culture was obtained Markedly distended loops of small bowel presented An intussusception was found, with the head of the intussusceptum in the descending colon Reduction was impossible without delivery, hence the intussusception was delivered, after which reduction was accomplished The intussusception was ileocolic in type, starting about 30 cm above the ileocecal valve The terminal ileum was markedly discolored However, later the color improved and the bowel appeared viable At the site where the intussusception began, there was present in the wall of the ileum, on its antimesenteric border, a small, hard, round, tumor-like mass about one centimeter in diameter There was puckering of the serosa over this mass The mass was excised longitudinally and the defect closed transversely, leaving a satisfactory lumen in the bowel There was no gross remnant of the omphalomesenteric duct The abdomen was closed in layers without drainage, and the patient was returned to the ward in fair condition

Following operation, the patient became dyspneic and cyanotic, the pulse rapid and weak, and the skin cold with perspiration Death occurred about two and one-half hours later, in spite of supportive treatment Blood donors could not be obtained Permission for autopsy was not granted

Pathologic Examination—*Gross* The surgical specimen consisted of a segment of small intestine, three centimeters in length, markedly discolored and apparently infarcted The serosal surface was dull and covered by a thin layer of fibrin, the wall was generally dusky and succulent, and the mucosal surface deeply discolored There was a bulbous thickening between the mucosa and serosa which on section showed a small tumefaction of muscular appearance, measuring 1.3 cm in its greatest diameter It did not appear to be sharply outlined *Microscopic* Sections taken through the nodule showed it to be composed of single and multiple groups of closely arranged duct-like and cystic spaces surrounded by irregularly arranged interlacing bands of smooth muscle Edematous

MYO-EPITHELIAL HAMARTOMA

fibrous tissue supported and engulfed the smooth muscle and epithelial-lined spaces and accounted for the considerable bulk of the tumor (Fig 1) About the periphery of the larger cyst-like spaces of bizarre outline, presenting intracystic papilliferous projections which tended to coalesce, were smaller, isolated duct-like spaces surrounded by smooth muscle. Smooth muscle formed the basement layer for the epithelium of the duct type in most instances. It did not appear to be an intrinsic part of the musculature of the intestinal wall, but possibly derived from the latter. The epithelium lining the duct structures was of the tall columnar undifferentiated type with eosinophilic cytoplasm and prominent basal nuclei, not unlike that of pancreatic duct epithelium in its appearance (Fig 2). In some instances the epithelium was crowded into a pseudostratified



FIG 1—Low power view of tumor showing the epithelial lined cyst like and duct like spaces surrounded by smooth muscle supported by edematous fibrous tissue

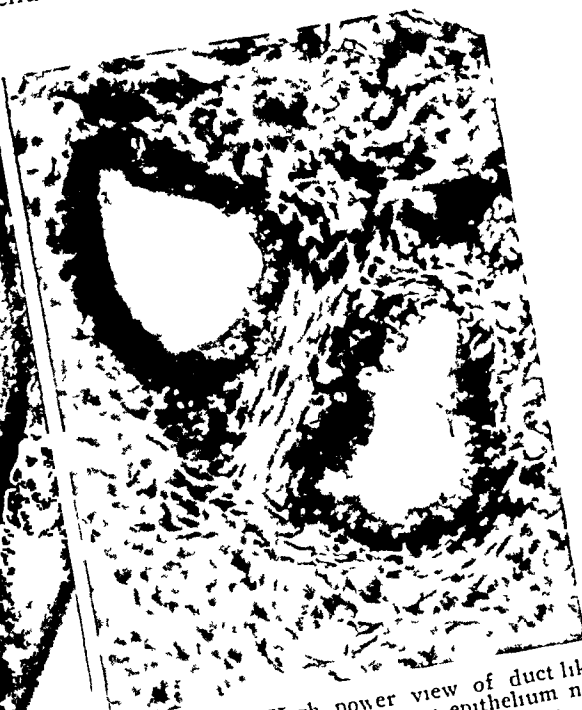


FIG 2—High power view of duct like spaces lined by tall columnar epithelium not unlike that of pancreatic duct epithelium

arrangement. At the bases of some papillary projections there were noted acinar-like structures whose lining cells showed clear cytoplasm and small compressed basal nuclei, suggesting an attempted formation of the Brunner-type gland, though this feature was not conspicuous. The epithelial-lined ducts and cystic spaces were observed to be immediately subjacent to the mucosa in some areas but communication of the latter with the lumen of the intestine was not demonstrated. The overlying mucosa showed necrosis, leukocytic infiltration and heavy surface exudation.

DISCUSSION—Tumors of developmental origin occurring along the gastrointestinal tract are most frequently described as occurring in the gastroduodenal region where mishaps in the complicated process of development are most apt to occur. They occur to a lesser extent, though rather commonly, along the lower intestine, particularly in the ileum and jejunum. The essential component tissues of such tumors are epithelium and smooth muscle though the latter has not been emphasized to the same degree as the former. Most often the epithelial elements show varying degrees of structural differentiation commonly toward pancreatic tissue, with or without duct-like structures lined by undifferentiated columnar epithelium. Hence the most common category

into which these tumors have been placed is aberrant or heterotopic pancreatic tissue. Islet tissue and Brunner-type glands have been reported as associated features in some cases. In those instances in which duct-like structures are the most conspicuous and the glandular differentiation less pronounced, or lacking, Lauche¹³ has suggested the term, "incompletely differentiated accessory pancreas." When duct-like structures usually lined by a single layer of undifferentiated columnar epithelium, in association with closely related smooth muscle, are found, the tendency has been to use the designation of adenomyoma,^{14, 15} indicative of neoplasia and the types of component tissues, though the ability of these tumors to grow has not been definitely proved.

It has been the tendency on the part of those interested in the explanation of the origin of such tumors to regard them as heterotopias of developmental origin, derived from misplaced epithelial buds or diverticula during the process of development of the intestinal tract. Several theories of origin of aberrant pancreatic tissue in the stomach and duodenum have been advanced. Zenker¹⁶ believed them to be anomalies of early life on the basis of an extra diverticulum from the duodenum. Glinski¹⁷ hypothesized failure of coalescence of one or more anlagen of the pancreas in cases of accessory pancreatic tissue in the duodenum. Warthin¹⁸ believed that lateral budding of the rudimentary pancreatic ducts occurred as they passed through the duodenal wall. Obviously these theories do not explain the occurrence of such aberrant tissue in remote sites such as the lower intestinal tract. Horgan¹⁹ suggested the possibility that branching buds of the pancreatic anlage came into contact with remote sites and became engrafted. Lauche¹³ reserved the term adenomyoma for heterotopias whose differentiation was not toward the pancreatic tissue type. King and MacCallum²⁰ explained the genesis of accessory pancreatic tissue in the stomach wall on the basis of a post-inflammatory sequela, following a study of four cases, all over 45 years of age, which cases presented demonstrable associated chronic inflammatory changes, apparent development by differentiation from gastric mucosa under inflammatory stimuli and direct connection of the glandular structure with atypical gastric mucosa. King and MacCallum²⁰ believed that the close association of the glands with smooth muscle and the failure to demonstrate any relation of the associated duct-like structures with the surface were factors against the cell rest theory of Cohnheim. Clarke¹¹ advocated that such localized tumors of the gastro-enteric tract of epithelial and smooth muscle composition, regardless of their relative proportions and the degree of structural differentiation, be regarded as myo-epithelial hamartomata. He saw no purpose in endeavoring to classify such occurrences, manifesting such broad structural differentiation, as to the type of tissue most closely simulated in the particular instance of this group. He believed that the mechanism of formation was on the basis of misplaced epithelium occurring during the stage of embryonal development of the tract, and that the smooth muscle was independent of the muscle of the intestinal wall but possibly derived from the latter in response to stimuli provided by misplaced epithelium.

The variation in the structural arrangement of the epithelium, ranging from undifferentiated duct type epithelium lining spaces to more specialized glandular formation embracing pancreatic and Brunner's-type acini or mixtures of these elements should be regarded as reflecting degree of differentiation, rather than dissimilar origin

We are in accord with Clarke's viewpoint and believe that the tumor in this case is best classified as a myo-epithelial hamartoma

SUMMARY

1 A tumor-like formation composed of epithelial-lined ducts and cystic spaces in intimate association with smooth muscle, of developmental origin, associated with intussusception in an infant, is reported

2 Justification for classification of the lesion as a myo-epithelial hamartoma is offered

REFERENCES

- ¹ King, E L Benign Tumors of the Intestines With Special Reference to Fibroma Surg, Gyn and Obs, **25**, 54, 1917
- ² Willis, A M Intussusception Resulting from Benign Tumor of the Intestine Surg Gyn and Obs, **30**, 603, 1920
- ³ Raiford, T S Tumors of the Small Intestine Arch Surg, **25**, 122, 1932
- ⁴ Moore, R M, and Schmeisser, H C Benign Tumors of the Small Intestine South Med Jour, **27**, 386, 1934
- ⁵ Cave, H W Tumors of the Small Intestine ANNALS OF SURGERY, **96**, 269, 1932
- ⁶ Joyce, T M Tumors of the Small Intestine ANNALS OF SURGERY, **100**, 949, 1934
- ⁷ Fiske, F A Intussusception due to Intestinal Tumors ANNALS OF SURGERY, **106**, 221, 1937
- ⁸ Goldberg, S A Unusual Neoplasms of the Small Intestines Am Jour Clin Path, **9**, 516, 1939
- ⁹ Cohn, S, Landy, J A, and Richter, M Tumors of the Small Intestine Arch Surg **39**, 647, 1939
- ¹⁰ Rankin, F W, and Newell, C E Benign Tumors of the Small Intestine Surg, Gyn and Obs, **57**, 501, 1933
- ¹¹ Clarke, B E Myoepithelial Hamartoma of the Gastro-Intestinal Tract Arch Path **30**, 143, 1940
- ¹² Albrecht, E Quoted by Mallory, Tracy, B New Eng Jour Med, **218**, 1105, 1938, and by Goldsworthy, N E, Jour Path and Bact, **39**, 291, 1934
- ¹³ Lauche, A Die Heterotopien des Ortsgehorigen Epithels im Bereich des Verdauungskanaals Virchow's Arch f path Anat, **252**, 39, 1924
- ¹⁴ Woolsey, J H, and Miltzner, R J Adenomyoma of the Stomach Arch Surg, **16**, 583, 1928
- ¹⁵ Stewart, M J, and Taylor, A L, Adenomyoma of the Stomach Jour Path and Bact, **28**, 195, 1925
- ¹⁶ Zenker, F A Nebenpankreas in der Magenwand Virchow's Arch f path Anat, **21**, 369, 1861
- ¹⁷ Glinski, L K Zur Kenntnis des Nebenpankreas und verwandter Zustände Virchow's Arch f path Anat, **164**, 132, 1901
- ¹⁸ Warthin, A S Two Cases of Accessory Pancreas Physician and Surgeon, **26**, 337, 1904
- ¹⁹ Horgan, E J Accessory Pancreatic Tissue Report of Two Cases Arch Surg, **2**, 521, 1921
- ²⁰ King, E S J, and MacCallum, P Pancreatic Tissue in the Wall of the Stomach Arch Surg, **28**, 125, 1934

A STUDY OF THE BACTERIOLOGY OF THE COMMON BILE DUCT IN COMPARISON WITH THE OTHER EXTRAHEPATIC SEGMENTS OF THE BILIARY TRACT

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PREVIOUS STUDIES of the bacteriology of the biliary tract have been restricted to investigations of the wall of the gallbladder and its contents, the regional nodes, and the duodenum. We can find no systematic study in the literature of the bacteriology of this region which has included the common bile duct of the same patients in whom the other portions were studied.

The following technic was employed in obtaining material for this study. Common duct bile was removed through the wall of the duct only in cases in which choledochotomy was to be performed. In the majority of cases it was obtained by introducing a cannula with an olive-shaped tip through the stump of the cystic duct. One or two cubic centimeter-specimens of common duct bile were then aspirated. This procedure has the advantage that it eliminates the possibility of damaging the wall of the common duct. However, it has the disadvantage of contaminating the common duct bile from the cystic duct. That this actually occurred in exceptional instances will be referred to later (Series III). As such contamination occurred rarely, we persisted in the use of this technic. In those instances in which the valves of Heister offered marked resistance to the passage of the cannula, the attempt to pass it was given up, in accordance with the principle of *primum non nocere*. For this reason, specimens of common duct bile were obtained in only 75 of 138 cases studied.

In addition to the common duct bile, specimens were obtained from the gallbladder and from the duodenum in all cases, as was a piece of the wall of the gallbladder. Whenever a sediment was obtained from the material, stained microscopic smears were prepared and cultures made on agar and in broth. Large quantities of broth were used in order to prevent any possible bactericidal action by the substrate on the bacteria being sought. The specimens from the wall of the gallbladder were taken from the fundus, passed through alcohol, and flamed several times. They were then triturated and placed in broth. Care was taken to prevent contamination. Aerobic gram-positive spore-forming bacteria frequently grew out. As yet, it has not been possible to judge exactly the origin and importance of these bacteria. In general, they did not appear in cultures of the gallbladder wall containing pathogenic bacteria, such as *B. coli*, streptococcus, and *B. typhi*. For the present, we are assuming that these organisms were contaminants.

The cystic lymph node was examined in several cases. In most instances it proved to be sterile and for this reason routine study of the node was discontinued.

All cultures were incubated for three days. The more extensive bacteriologic technics were not employed because the object of the study was not to gain more knowledge of the bacteria causing inflammation of the biliary tract, but rather to make a comparative bacteriologic study of the extrahepatic segments of the biliary tract, and particularly of the bacteriology of the common bile duct in comparison with that of the other segments. Table I gives a general orientation on the results obtained from the bacteriologic studies. The flora of the common bile duct, in comparison with that of the other segments, is emphasized in the table by the numerical occurrence of the different possibilities. The significance of the relationships shown in the table are then discussed in the same order in which they are presented.

Series I—In this group, not only was the culture of the common duct bile negative, but also the cultures of the gallbladder bile, the gallbladder wall, and the duodenal contents, were sterile. There was 25 such cases. Twenty of these cases were instances of uncomplicated chronic calculous cholecystitis, atrophic sclerosing cholecystitis, or hydrops of the gallbladder. Three were cases of uncomplicated hydrops of the gallbladder, with stones. One case (No. 88) had a calculus lodged in the papilla of Vater, in addition to a chronic calculous cholecystitis, and the remaining case was that of a patient who was operated upon for adhesions following a previous cholecystectomy. It is evident, therefore, that 23 of the 25 cases of general sterility are cases of uncomplicated gallbladder disease, such as chronic calculous cholecystitis, or hydrops of the gallbladder. In Case No. 88, in which there was a calculus in the papilla of Vater, the common duct bile was sterile and of normal appearance, as were the other samples. The cases comprising Series IV show that in all cases of common duct stone there is bacterial infection of the common duct bile, with some change in its appearance. The fact that there was no infection of the choledochal bile in Case No. 88 seems to indicate that the passage of the calculus from the gallbladder toward the duodenum had occurred so recently that functional or organic alterations had not as yet been produced by the calculus.

TABLE I

COMPARATIVE RESULTS OF BACTERIOLOGIC EXAMINATIONS OF BILE FROM THE COMMON BILE DUCT WALL AND CONTENTS OF THE GALLBLADDER AND DUODENAL JUICE—TOTAL NUMBER OF CASES EXAMINED—75

Choledochal Bile <i>without</i> Bacteria—41 cases		Choledochal Bile <i>with</i> Bacteria—34 cases	
The other cultures (—)—25	The other cultures (+)—16	The other cultures (—)—0	The other cultures (+)—34
			Without lithiasis of the common bile duct—18
			With lithiasis of the common bile duct—16
Reference in course of the article		Series III	Series IV
Series I	Series II		
Key: Sign minus (—) = <i>without</i> bacteria			
Sign plus (+) = <i>with</i> bacteria			

Series II—In the cases in this series the common duct bile was sterile whereas the other samples, namely, the wall and bile of the gallbladder and the duodenal juice, were contaminated by bacteria. There were 16 such cases which are described in detail in Table II. Before analyzing the data in this

table, it is advisable to make a rough comparison of the data in Series II, III, and IV as they appear in Tables II, III, and IV. When this is done, a remarkable irregularity of the bacteriologic findings in Table II will be noted. If the two cases of choledocal lithiasis (Nos 45 and 32) are excluded, there remain only two cases (Nos 8 and 111) in which the bacterial flora was the same in the three different specimens (gallbladder bile, gallbladder wall, and duodenal juice). In contrast to this, the flora was the same in most of the

TABLE II
CHOLEDICAL BILE (—) CULTURES OF OTHER STRUCTURES OF THE BILIARY
SYSTEM (+)—TOTAL NUMBER OF CASES 16
SERIES II

No of the Case	Operative Diagnosis	W	G	D	Macroscopic Alterations of Choledocal Bile
56	Chronic calculous cholecystitis	Cn	—	Enterococ & <i>Staphylo alb</i> Agar broth	○
84	Chronic calculous cholecystitis	Cn	Agar broth Cn	Enterococ and yeasts	○
85	Chronic calculous cholecystitis	Cn	Cn	Associated bact	○
122	Chronic calculous cholecystitis	Cn	<i>B. pyocyaneus</i>	/	○
111	Sclerosing atrophic calculous cholecystitis	Coliform bact	Coliform bact	Coliform bact	⊙
8	Sclerosing atrophic calculous cholecystitis	Associated bact flora	Associated bact flora	Associated bact flora	○
	Cysticoduodenal fistula	—	Enterococ	<i>B. coli</i>	⊙
87	Suppurative cholecystitis	Cn	—	<i>B. coli</i> and staphylococ	○
14	Calculous empyema of gallbladder	Staphylococ	—	—	/
A	Calculous empyema of gallbladder	Cn Enterococ	—	—	○
50	Hydrops of calculous gallbladder, peri- cholecystitis and chronic appendicitis	Enterococ	—	—	⊙
37	Hydrops of calculous gallbladder and appendicular peritonitis	<i>B. coli</i>	—	—	○
30	Chronic calculous cholecystitis and dyskinesia	—	Gram pos cocci Cn?	Staphylococ and Sarc	●
20	Chronic calculous cholecystitis, stenosing odditis and angiocholitis?	Cn Streptococ	—	/	●
				Staphylococ Enterococ	○
36	Stenosing odditis, pancreatic stricture	/	/	—	○
45	Chronic calculous cholecystitis and choledocal lithiasis	<i>B. coli</i>	<i>B. coli</i>	<i>B. coli</i>	○
32	Calculous empyema of gallbladder, solitary secondary choledocal lithiasis	<i>B. coli</i>	<i>B. coli</i>	<i>B. coli</i>	○
Key	Cn = contamination, / = not examined, (—) = without bacteria, (+) = with bacteria, ○ = with out macroscopic alteration, ⊙ = slight macroscopic alterations, ● = acute macroscopic alterations, W = wall of gallbladder, G = bile of gallbladder, C = choledocal bile, and D = juice of duodenum				

cases in Series III and IV. Furthermore, in the cases in Series II the bacteria of moderate virulence were predominant and bacterial contamination was frequent. It is quite probable that many of the bacteria identified were not the active causal agent of the disease and that these cases really belonged in the first series in which the bile of the common duct and of the other parts of the extrahepatic biliary system was sterile. In three cases (Nos 20, 30 and 36) the choledocal bile was sterile in the presence of stenosing odditis or dyskinesia which were verified by cholangiography during operation. Thus, it seems that bile stagnation does not necessarily give rise to infection of the choledocal bile, not even in cases where microscopic alterations

of the bile exist (Nos 20 and 30) In this series there were two cases (Nos 32 and 45) in which the choledocal bile was sterile and of normal appearance in the presence of calculi It is probable that the sterility of the choledocal bile in these two cases could be explained in the same way as in Case No 88 in Series I The fact that the common duct bile was sterile in these cases in which cultures of the wall and bile of the gallbladder and of the duodenal

TABLE III
CHOLEDOCAL BILE (+) CULTURES OF OTHER STRUCTURES OF THE BILIARY SYSTEM (+)
COMMON BILE DUCT WITHOUT CALCULI Total number of cases 18

SERIES III

No of the Case	Operative Diagnosis	W	G	C	D	Macroscopic Alterations of Choledocal Bile
16	Chronic calculous cholecystitis	<i>B proteus</i>	<i>B proteus</i>	<i>B proteus</i>	<i>B proteus</i>	⊙
19	Chronic calculous cholecystitis	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	⊙
27	Chronic calculous cholecystitis	<i>B typhi</i>	<i>B typhi</i>	2 colonies of <i>B typhi</i> Agar broth	<i>B typhi</i>	○
100	Chronic calculous cholecystitis	Enterococ	Enterococ	Enterococ	Enterococ	○
108	Chronic calculous cholecystitis	<i>B coli</i>	<i>B coli</i>	2 colonies of <i>B coli</i>	<i>B coli</i>	○
116	Chronic calculous cholecystitis	Streptococ	Streptococ	3 colonies of streptococ	Streptococ	○
113	Sclerosing, atrophic calculous cholecystitis	Cn	<i>B coli</i>	Agar broth <i>B coli</i>	<i>B coli</i>	○
129	Sclerosing atrophic calculous cholecystitis	Cn Enterococ	Enterococ	2 colonies of enterococ	Enterococ	⊙
72	Sclerosing atrophic calculous cholecystitis Empyema	<i>B pyocyaneus</i>	<i>B pyocyaneus</i>	Isolated colonies of <i>B pyocyaneus</i>	<i>B pyocyaneus</i>	○
79	Chronic cholecystitis without concretions	<i>B coli</i>	<i>B coli</i>	<i>B coli</i> (small number)	<i>B coli</i>	⊙
66	Chronic calculous cholecystitis and pericholecystitis	<i>B typhi</i>	<i>B typhi</i>	<i>B typhi</i>	<i>B typhi</i>	⊙
11	Chronic cholecystitis, without concretions and pericholecystitis	Cn	Enterococ	Enterococ	Enterococ	●
114	Chronic cholecystitis, without concretions and pericholecystitis	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	●
120	Sclerosing atrophic cholecystitis without concretions, hepatitis and appendicitis	/	Agar broth <i>B coli</i>	<i>B coli</i>	/	●
102	Chronic calculous cholecystitis, dyskinesia	Staphylococ	Streptococ <i>B coli</i>	<i>B coli</i>	<i>B coli</i>	○
92	Chronic calculous cholecystitis, stenosing odditis	/	/	Enterococ	/	○
63	Sclerosing atrophic cholecystitis without concretions and stenosing pancreatitis	Enterococ	Enterococ	Enterococ	Enterococ	⊙
73	Hydrops of calculous gallbladder and stenosing pancreatitis	Staphylococ	—	Agar broth Staphylococ	Agar broth Staphylococ	⊙

Key See those appended to Table II

juice contained pathogenic bacteria of identical species tends to show the strong bactericidal power of the choledocal bile, which may be sterile in the presence of infection in all the other extrahepatic segments of the biliary tract

Series III—The 18 cases in this series yielded specimens which were infected in every instance In none of the cases however, were there stones in the common duct The uniformity of the bacteriologic results in the different parts of the biliary system in the third and fourth series is sig-

nificant and tends to verify the etiologic role of the identified bacteria in the development of the pathologic process. There are, however, certain quantitative bacterial differences between the choledocal bile and the other specimens which do not exist in the cases of the first and second series. They are of significance especially because they were seen only in uncomplicated processes in the gallbladder, generally associated with sterility of the choledocal bile. Cases 27, 100, 108, 113, 116 and 129 are of particular interest in this regard and Cases 72 and 79 may also be considered. A heavy layer of bacteria grew on agar cultures of the wall and bile of the gallbladder and of the duodenal juice, whereas only isolated colonies of bacteria developed in cultures of the choledocal bile prepared with the same amount of material as that used in the other cultures. We believe that contamination of the choledocal bile, rather than actual infection would give a plausible explanation for the scantiness of the growth in these cultures. The growth probably occurred because some of the large number of bacteria which were present in other parts of the biliary system were introduced into the common duct bile at the time the cannula was passed through the stump of the cystic duct. Further support is given to this interpretation by the fact that the choledocal bile had a normal microscopic appearance in six of the eight cases of this nature in Series III, whereas it was more or less altered in six of the eight complicated cases (Nos 63, 66, 73, 102, 114 and 120) in the same series. There was organic or functional stagnation in four of these cases (Nos 63, 73, 92 and 102). These cases were complicated by dyskinesia, stenosing odditis and stenosing pancreatitis. Infection was present in these cases, and the macroscopic appearance of the common duct bile was normal in Cases 92 and 102 and altered in Cases 63 and 72.

Series IV—This series comprised 16 cases with infection of the common duct bile, accompanied by common duct stones. The wall and bile of the gallbladder and the duodenal juice were infected. Details are presented in Table IV. The bile of the common duct was infected in all cases with choledocal lithiasis, except Case No 88 of the first series, in which the calculus was lodged in the papilla of Vater and in Cases No 32 and 45 of the second series. In the 16 cases in the fourth series with common duct stones, the bacteria were of the same type as that identified in the wall and bile of the gallbladder and in the duodenal juice. This is taken as evidence that the bacteria recovered had an etiologic role in the development of the infection. The clinical records show that the macroscopic appearance of the common duct bile was more or less altered in all the cases of this series.

Previous investigations, by various authors, have shown that suppuration within the gallbladder frequently results in autosterilization of the gallbladder contents. This may occur especially in cases of inflammatory edema at the neck of the gallbladder, which causes occlusion. The fact that bacterial infection of the vascular bile existed previously can often be concluded from stained preparations, which show bacterial rests within a large number of cells. Even when the stained preparations show bacteria with well preserved

BACTERIOLOGY OF COMMON BILE DUCT

TABLE IV

CHOLEDOCAL BILE (+) CULTURES OF OTHER STRUCTURES OF BILIARY SYSTEM (+)
CALCULI IN THE COMMON BILE DUCT Total number of cases 16

SERIES IV

No of the Case	Operative Diagnosis	W	G	C <i>B coli</i> Enterococ Staphylococ bact	D <i>B coli</i> Enterococ	Macroscopic Alterations of Choledocal Bile
133	Chronic calculous cholecystitis, choledocal lithiasis	Cn	/		/	●
95	Chronic calculous cholecystitis, choledocal lithiasis	/	/	<i>B coli</i>	/	◎
22	Chronic calculous cholecystitis, multiple secondary lithiasis	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	◎
52	Sclerosing atrophic chronic cal- culous cholecystitis, solitary choledocal lithiasis, chronic ap- pendicitis	Enterococ	Enterococ	Agar broth Enterococ	—	◎
13	Sclerosing, atrophic chronic cal- culous cholecystitis, multiple choledocal lithiasis	/	<i>B coli</i> Agar broth 48 hours	<i>B coli</i>	<i>B coli</i>	◎
77	Sclerosing atrophic, chronic chole- cystitis without concretions, soli- tary choledocal lithiasis	/	<i>B coli</i>	<i>B coli</i>	/	●
51	Sclerosing atrophic cholecystitis, multiple choledocal lithiasis	/	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	●
128	Chronic calculous cholecystitis, multiple secondary choledocal lithiasis	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	◎
93	Chronic calculous cholecystitis, choledocal lithiasis, stenosing odditis	<i>B coli</i>	<i>B coli</i>	Isolated colonies of <i>B coli</i>	<i>B coli</i>	◎
101	Chronic calculous cholecystitis, choledocal lithiasis, stenosing odditis	Cn	<i>B coli</i>	<i>B coli</i>	<i>B coli</i>	/
90	Chronic calculous cholecystitis, choledocal lithiasis, stenosing pancreatitis	/	Isolated colonies of <i>B coli</i>	<i>B coli</i>	<i>B coli</i>	●
130	Chronic calculous cholecystitis, choledocal lithiasis, stenosing pancreatitis	/	/	Streptococ	/	●
48	Chronic calculous cholecystitis, multiple secondary choledocal lithiasis, stenosing odeditis	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	●
39	Perforated calculous cholecystitis, secondary choledocal lithiasis	Enterococ Staphylococ	—	Enterococ	Isolated colonies of enterococ	◎
81	Chronic calculous cholecystitis, soli- tary calculous of hepatic duct	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	◎
57	Multiple choledocal lithiasis with recurrences after cholecystectomy and choledocotomy	/	/	<i>B coli</i> Enterococ	<i>B coli</i> Enterococ	●
Key See those appended to Table II						

staining properties, the cultures frequently remain sterile, whereas in other parts of the biliary system, bacteria of the same type may be recovered. Illustrations of this type of autosterilization, either partial or complete, occurred in Cases No 39, 77, and 90 of the fourth series, in Cases No 73, and 120 of the third series, and in Cases No 14 and 20 in the second series.

Quantitative differences between bacteria in the common bile duct and in other parts of the biliary system were observed infrequently in the presence of choledocal calculi (Cases No 52 and 93).

CONCLUSIONS

1 Choledocal bile is sterile in a large number of patients with disease of the extrahepatic bile ducts. In our operative material this occurred in 41 of 75 cases, or 54.7 per cent. If a correction is made for cases in which bacterial contamination was probable, the figure would be 64 per cent.

2 Sterility of the choledocal bile is especially frequent in cases of uncomplicated chronic calculous cholecystitis and atrophic sclerosing cholecystitis and was observed in 25 to 34 such cases, or 73.5 per cent. Since the possibility of contamination could not be excluded in seven of the ten remaining cases of uncomplicated cholecystitis in the third series, the frequency of sterile common duct bile in such cases may be about 91 per cent. The results were similar in cases of empyema, or hydrops of the gallbladder, when the gallbladder was the only organ involved by the disease. On the other hand, the choledocal bile was frequently infected when there were complications, either of an organic nature, such as pericholecystitis, hepatitis, odditis, or of a functional nature, such as dyskinesia.

3 Stagnation of the choledocal bile, resulting from dyskinesia, or stenosing odditis, in the absence of stone, resulted in infection of the common duct bile in four of seven cases. In the remaining three cases actual infection was not observed, although macroscopic alterations of the choledocal bile existed.

4 Stones in the common duct were the most frequent cause of infection of the choledocal bile. Infection occurred in 16 of 18 cases of choledocal lithiasis, or 88.8 per cent. In the two remaining cases, the choledocal bile did not contain bacteria and had a normal macroscopic appearance. It seemed probable that in these two cases the calculus found during the operation in the common duct was migrating from the gallbladder to the duodenum. Probably, it is only under these circumstances that the choledocal bile may be sterile in the presence of common duct stones. The predominant bacteria in the various parts of the biliary system were *B. coli*, which occurred 72 times, and streptococcus, which occurred 49 times. Other bacteria recovered were *B. typhi* (eight times), *B. pyocyaneus* (four times), and staphylococcus, saprophytes, and associated bacteria (13 times).

5 Bacterial infection of the common duct is always associated with infection of the other parts of the biliary system and the bacteria found are generally of the same species.

6 The choledocal bile appears to have strong bactericidal power. This finding is striking and of great practical importance.

We hope that similar bacteriologic studies will be undertaken in other clinics.

The operative material was obtained in the Clinical Ward of the Surgical Clinic, of the Faculty of Medicine, of the Universidad Nacional de Cordoba, Argentina, of which Prof. Pablo L. Mirizzi is the head. The bacteriologic researches were made in the Bacteriologic Laboratory, of the Chair of Pediatrics, of Prof. Jose M. Valdes, of which the author is the head.

The details of the technic appear on page 177 of Vol. 5 of *Actas y trabajos* of the Sixth National Congress of Medicine, which was held in Cordoba, October 16-21, 1938.

ACUTE PANCREATITIS

REPORT OF TWENTY-NINE CASES

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ACUTE PANCREATITIS is a bizarre disease difficult to diagnose, and easy to confuse with any other of the many acute intra-abdominal conditions. In its severest form it is a serious and not infrequently fatal ailment. The first accurate description and presentation of acute pancreatitis as a clinical entity was given by Reginald Fitz,¹ in 1889, when he published a report of 15 cases. Only two of these patients recovered. Fitz clearly described the hemorrhagic destruction of the pancreas and the associated fat necrosis, and felt that it was due to a gastro-enteritis extending up the pancreatic duct. Opie² demonstrated, in 1901, that retrograde injection of the pancreatic duct with bile produced a fatal pancreatitis in dogs. An important contribution was made by Wohlgemuth,³ in 1910, when he reported that in irritative conditions of the pancreas, the pancreatic ferments can be demonstrated in increased amounts in the urine and blood. In 1934, Mikkelsen⁴ presented a series of cases, with a mortality of 75 per cent by the conservative treatment of pancreatitis. This was such a low mortality as compared with the then recognized mortality of 40 to 50 per cent⁵ that his figures were looked upon with skepticism. Mikkelsen used the diastase test as the main criterion for diagnosis and, therefore, included milder cases in which the diagnosis otherwise might never have been made. Since this stimulating work, several papers^{6, 7, 8, 9, 10, 11} have been published which tend to confirm his contentions and to substantiate his principles of conservative management of patients with acute pancreatitis.

The data which is herewith presented represents the results of our study of this subject on the Surgical Services and in the Hall Wilson Laboratory of the Hartford Hospital, from September 1, 1938, to December 31, 1941.

MATERIAL—The clinical material has been taken from the private and ward surgical services, and includes patients in whom the diagnosis has been made by operation, autopsy, or clinical evidence associated with an elevated urinary diastase. We have used the method of diastase determination described by Foged¹² and have found it very satisfactory. Foged's diastase determination depends upon the hydrolyzation of starch by measured dilutions of urine. The mixture is incubated and then iodine is added to determine the starch free tubes. The diastase activity is expressed in units of which one unit is arbitrarily taken to be the amount of diastase necessary to hydrolyze 1 cc of 0.1 per cent starch solution under standard conditions. Normal urine shows a diastase activity of less than 300 units. A finding above this

is abnormal and indicates an acute irritative pancreatic process. We have observed no proven false positives as every case operated upon in the acute stage of the disease, on whom the test has been made early, has shown an elevated diastase. It should be emphasized that the test must be made early in the disease, and fresh urine should be used (Chart I) as the activity of

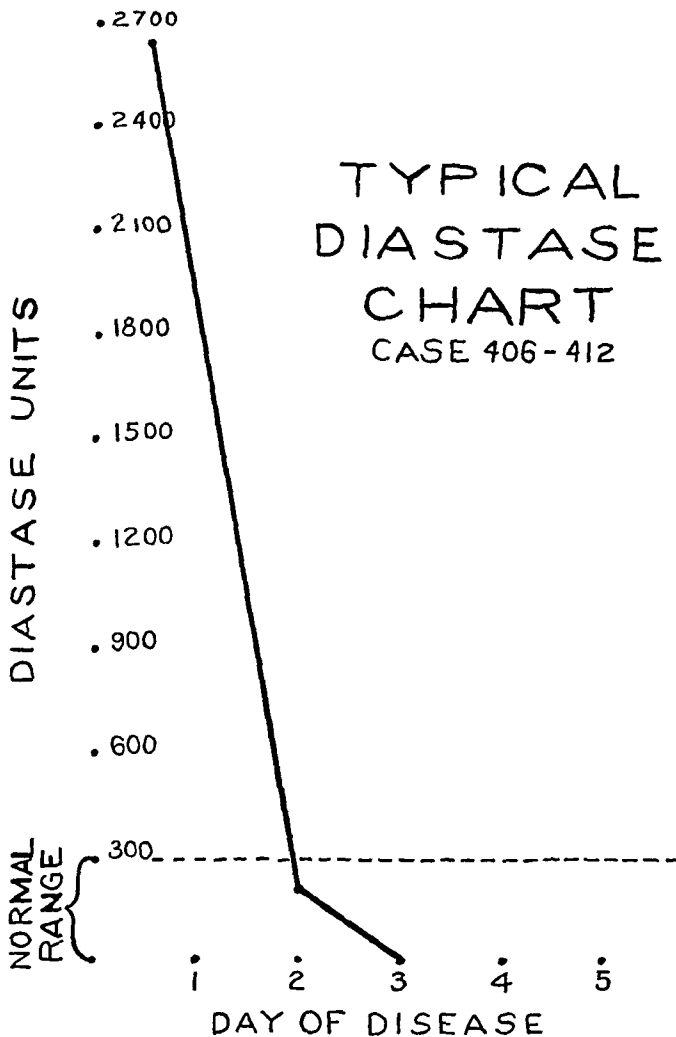


CHART I

the enzyme deteriorates on standing. We have used the urine rather than the blood because it is simpler to obtain, requires less manipulation in the laboratory, and we feel gives accurate results.

Symptoms and Findings—In a little over three years, there were 29 patients seen in the Hartford Hospital with acute pancreatitis. The severity of the illness varied from a rather mild abdominal upset to an overwhelming and sometimes fatal illness. The onset was usually abrupt with upper abdominal pain accompanied by nausea with vomiting. The pain often radiated to the back. Jaundice sometimes was present. The physical findings varied in degree but consisted chiefly of upper abdominal tenderness and spasm. High epigastric tenderness was present in many cases and not infrequently,

left flank tenderness The initial temperature ranged from 99° to 103° F and the pulse from 60 to 160 The leukocyte count was over 15,000 in nine patients and above 10,000 in 19 patients The urine analysis is of special interest, as 16 out of the 29 showed two plus and three plus albumin a finding which is not generally emphasized and which undoubtedly reflects the severity of the disease Gallstones were present in 14 surgical patients and there was roentgenographic evidence of their presence in two not operated upon, making a total of 55 per cent In nine, the gallbladder was normal at operation or roentgenographically, while in four patients there was no data given The patients ranged in age from 23 to 79 years, with an average age of 49 There were 21 women and eight men Table I shows the incidence of the various symptoms and findings

TABLE I
SUMMARY OF CHIEF SYMPTOMS AND FINDINGS

1	Duration of symptoms 24 hours or less	19
2	Nausea and vomiting	18
3	Temperature 101° F, or over	18
4	Urine albumin two plus or over	16
5	Gallstones present	16
6	Leukocyte count over 15,000	9
7	Icteric index over 15	7

Diagnosis—The diagnosis of pancreatitis has been made in the acute surgical patients by the finding of wine-colored fluid or fat necrosis in the presence of a thickened pancreas In the patients not subjected to operation the diagnosis has been reached by the clinical manifestations and the finding of a urinary diastase of 300 or more Foged units The test has been accurate in our experience, and in the cases where early operation has been performed we have had no patients with a positive test in whom there has not been evidence of pancreatitis In the patients operated upon one or two weeks after the onset, the process had regressed so that gross pathologic evidence of pancreatitis was not present In the group of patients undergoing delayed operations, some as long as 16 days from the acute onset, the diagnosis has been made by the same criteria used in the nonoperative cases The three delayed cases, operated upon from four to eight days from the onset of their illness, showed wine-colored fluid or fat necrosis while the seven cases operated upon from nine to 16 days after the onset had neither fluid nor fat necrosis

Cases of elevated diastase have been reported in patients with peptic ulcers which penetrate into the pancreas⁸ and in mumps¹¹ pancreatitis No cases of this type were observed in this series

Treatment—The method of treatment divided itself into three distinct groups of cases 1 Those having immediate operation 2 Those having a delayed operation 3 Those having no operation Nine patients were operated upon as an emergency procedure within the first 72 hours of the disease ten were operated upon later from the fourth to 16th day of their illness and ten had no operation There were four deaths in the entire group

giving a gross mortality of 14 per cent. Three of these deaths occurred in the patients who were subjected to immediate operation, giving a mortality of 33 per cent for that group. The fourth death was in the nonoperative group, and occurred in a diabetic patient who died in uncontrollable diabetic coma, and at autopsy was found, to everyone's complete surprise, to have a *fulminating pancreatitis*. In the nine cases of immediate operation the correct diagnosis was not made before operation, and the following preoperative diagnoses were given: Acute cholecystitis, 4, perforated peptic ulcer, 2, chronic cholecystitis, 1, twisted ovarian cyst, 1, and acute appendicitis, 1. In the patients operated upon later, the preoperative diagnosis of acute pancreatitis was made once, and substantiated by finding fat necrosis, in the remaining cases the diagnoses were either acute or chronic cholecystitis, which were correct, as in most instances the pancreatitis had subsided at the time of operation.

The severity of the disease is a most important factor in the outcome of the patient and, in order to evaluate our operative and nonoperative results more accurately, an attempt was made to group the cases into the classifications "severe" or "mild." Patients who had three out of four of the following findings were considered severe: A temperature over 101°F, a pulse about 100, a leukocyte count over 10,000, and a urine showing two plus albumin or greater. Those not having three of the above findings were classed as mild. In the immediate operative group, five were severe, in the delayed group, four were severe, and in the nonoperative group, four were severe, so that, in all, 41 per cent of the cases were severe. Tables II, III, and IV show the classification data, the diastase level, and the type of operation performed.

Complications—There were two cases of pancreatic cysts in this group. One was in a nonoperative patient, and reached the size of a small grapefruit in the left upper abdomen, and then spontaneously subsided. The other patient returned to be operated upon five months after her initial attack, the cyst was marsupialized, and she made a satisfactory recovery. There was one case of residual intra-abdominal sepsis which finally drained through in the original drainage wound. One patient had two attacks of pancreatitis and finally, on a third admission, cholecystotomy was performed during a quiescent period of his disease.

Discussion—There is no doubt that progress has been made in the diagnosis and in the treatment of acute pancreatitis. It is becoming more and more evident that hasty operative intervention in the very acute phase of the disease is a hazardous procedure. The evidence at hand of a 33 per cent mortality in the immediate operative group, and a 5 per cent mortality in combined nonoperative and delayed operative groups should make the surgeon deliberate carefully before contemplating celiotomy in acute pancreatitis. The diastase test is of invaluable assistance in arriving at a diagnosis. If operation is necessary it is best undertaken during the less severe phase of the disease, for the drainage of residual abscess

ACUTE PANCREATITIS

TABLE II
OPERATIONS WITHIN 72 HOURS FROM ONSET OF SYMPTOMS
Recovered 6—Died 3

History Number	Age	Temperature 101° F	Pulse Plus	W B C 10,000	Albumin 2—Plus	Urine Diastase Units	Duration before Operation	Operation	Result
SEVERE									
412-968	72	101	100	Not made	2 plus	380	2 hours	Drain to pancreas	
389-017	48	103	100	27,000	1 plus	600	12 hours	Cholecystostomy	
357-761	57	101	120	34,000	3 plus	Not made	24 hours	Cholecystostomy	Died
								Drain to pancreas	
386-499	38	101	100	15,900	2 plus	570	72 hours	Abdomen drained	Died
365-156	51	103	160	15,800	2 plus	1020	24 hours	Drain to pancreas	Died
MILD									
387-952	44	98.6	80	31,000	2 plus	240*	6 hours	Cholecystectomy	
371-566	41	101	90	19,950	0	540	48 hours	Cholecystectomy	
375-098	52	102	80	19,000	1 plus	120*	24 hours	Appendicectomy	
374-403	53	98	100	Not made	2 plus	Not made	6 hours	Cholecystectomy	

*Test made six days postoperative

Note Fat necrosis or wine colored ascitic fluid was found at operation in all of the above cases

TABLE III
OPERATIONS AFTER 72 HOURS FROM ONSET OF SYMPTOMS
Recovered 10—Died 0

History Number	Age	Temperature 101° F	Pulse Plus	W B C 10,000	Albumin 2—Plus	Urine Diastase Units	Duration before Operation	Operation
SEVERE								
416-448	61	101	100	8,500	2 plus	540	8 days	Cholecystectomy
393-054	27	102	120	10,500	3 plus	2,400	4 days	Cholecystectomy
387-537	23	101	100	20,200	2 plus	600	8 days	Cholecystectomy
364-896	47	102	100	14,200	2 plus	1,020	9 days	Cholecystectomy
MILD								
372-379	39	103	110	5,400	1 plus	960	16 days	Cholecystectomy
								Choledochostomy
360-675	57	99	70	11,900	1 plus	120*	4 days	Drain to pancreas
414-522	79	100	90	13,500	2 plus	300	15 days	Cholecystostomy
418-868	23	100	100	11,500	1 plus	2,400	16 days	Cholecystostomy
387-386	60	100	80	9,300	1 plus	1,275	4 days	Cholecystostomy
383-329	44	101	90	5,600	1 plus	1,020	11 days	Cholecystectomy
								Choledochostomy

*Test made ten days postoperative Fat necrosis found at operation

TABLE IV
NONOPERATIVE CASES
Recovered 9—Died 1

History Number	Age	Temperature 101° F	Pulse Plus	W B C 10,000	Albumin 2—Plus	Urine Diastase Units	Duration before Entry	
SEVERE								
381-998	59	103	100	19,000	1 plus	480	10 hours	
423-159	57	102	100	not made	2 plus	540	11 days postop †	
406-412 { *	58	101	100	11,300	0	2640	5 hours	
399-186 }								
359-529 ‡	54	100.5	110	not made	2 plus	not made	not given	Died
MILD								
412-433	60	100	70	12,800	2 plus	1020	5 days	
397-891	62	100	120	8,400	3 plus	2100	24 hours	
415-089	36	101	120	9,300	1 plus	2250	48 hours	
363-601	23	102	86	10,300	0	630	24 hours	
371-825	40	99	90	10,850	2 plus	510	7 days	
399-186	58	103	100	8,000	1 plus	1800	4 hours	

*Patient had two admissions both for pancreatitis

†Due to severe diabetes with coma, this patient failed to show the normal systemic reactions to her disease
Diagnosis made at autopsy

‡Patient developed an acute pancreatitis during convalescence from cholecystectomy

or cyst The frequent association of pancreatitis with cholecystitis often leads to later operations upon the gallbladder and bile ducts

SUMMARY AND CONCLUSION

1 Twenty-nine cases of acute pancreatitis seen at the Hartford Hospital, from September 1, 1938 to December 31, 1941, have been presented

2 In the cases subjected to immediate operation the mortality was 33 per cent

3 In the patients treated with delayed operation and without operation the mortality was five per cent

4 Conservative management in cases of acute pancreatitis is recommended

REFERENCES

- ¹ Fitz, R H Acute Pancreatitis Boston Med and Surg Jour, 120, 205-229 1889
- ² Opie, E L Disease of the Pancreas 1903—J B Lippincott Co, Philadelphia
- ³ Wohlgemuth, J Contributions on Functional Diagnosis of the Pancreas Berl klin Wchnschr, 47, 92-95, January 17, 1910
- ⁴ Mikkelsen, Otto Acute Pancreatitis Acta chir Scandin, 75, 373-415, 1934
- ⁵ Henderson, F F, and King, E S A Acute Pancreatitis Arch Surg, 30, 1049-1057, 1935
- ⁶ Lum, R Diagnosis and Conservative Treatment of Acute Pancreatitis N E Jour of Med, 219, 881-885, December 1, 1938
- ⁷ Fallis, L S, and Plain, G Acute Pancreatitis Surgery, 5, 358-373, March, 1939
- ⁸ Lewison, E F Acute Pancreatitis Arch Surg, 41, 1008-1037, October, 1940
- ⁹ Lewison, E F The Clinical Value of the Serum Amylase Surg, Gynec, and Obst, 72, 202-212, February, 1941
- ¹⁰ Abell, I Acute Pancreatitis Surg, Gynec & Obstet, 66, 348-353, February 15, 1938
- ¹¹ Elman, R Surgical Aspects of Acute Pancreatitis J A M A, 118, 1265-1270, April 11, 1942
- ¹² Foged, J The Diagnostic Value of Urine Diastase Am Jour Surg, 27, 439-446, March, 1935

PULMONARY ABSCESS—A SURGICAL PROBLEM*

CLASSIFICATION OF CASES AND DISCUSSION OF SURGICAL TREATMENT

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PULMONARY ABSCESES are commonly classified as acute or chronic, the distinction between the two being made solely on the basis of time. This practice has led to much confusion because the terms, acute and chronic, are vague in themselves and because the interval of time chosen to separate the two varieties of abscess represented by these terms is not always the same. Confusion is seen especially in the interpretation of statistics which are supposed to show the difference in the results of treatment between the so-called acute and chronic types. My belief that a pathologic classification is of far greater value than a clinical one, and that I could show this by analyzing the experience gained in treating 78 patients, has prompted me to prepare this report. Furthermore, it has been my feeling for some time that exact pathologic differentiation of pulmonary abscess deserved greater emphasis because of the satisfactory results which are now being obtained by lobectomy in an increasing number of selected cases. In this report, my cases have been divided into two main groups which are designated *uncomplicated* and *complicated*. By definition, a case was considered *uncomplicated* when there was only one abscess and this was unassociated with empyema, notable fibrosis, bronchiectasis or other serious complications. When there were multiple abscesses, empyema or pyopneumothorax, notable fibrosis, bronchiectasis, or other more rare complications such as suppurative pericarditis and suppurative mediastinitis, the cases were classified as complicated.

By *multiple abscesses* is meant two or more separate and distinct abscesses, or multiple cavities, in the same part of a lung which are connected by such small channels that something more than a simple unroofing operation was required in order to open them. The term does not necessarily imply secondary abscesses because occasionally two or more abscesses develop simultaneously in different parts of the same lung, or in both lungs.

The *empyemata*, all proved by operation, were recognized as complications of co-existing abscesses only when the clinical or roentgenologic evidence of abscess was unmistakable, or when an abscess was demonstrated at operation or subsequently during the postoperative course.

Notable fibrosis was assumed to be present when operation revealed an epithelialized cavity with rigid, irregular wall and multiple fistulae (so-called "*gitter lunge*") or when a cavity with rigid wall was found in a case with or without roentgenologic evidence of fibrosis, such as shrinkage or atelectasis of the involved lung, with displacement of the mediastinum and fixation of the chest wall.

Bronchiectasis was considered to be present only when it was demonstrated by bronchography or by direct examination of material removed at operation or necropsy. For the

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sake of simplicity, the patients with more than one complication were classified under only one heading, preference being given to the complications present in the following order: Bronchiectasis, empyema, multiple cavities, and notable fibrosis.

The division of abscesses into uncomplicated and complicated groups on the basis of pathology, is contrary to the common practice of classifying them as "acute" and "chronic," on the basis of duration of symptoms. According to this, the usual classification, an acute abscess is one of short duration with a wall composed of soft, necrotic tissue, whereas a chronic abscess is one of longer duration which is surrounded by a dense zone of fibrous tissue, with, in most instances, some degree of shrinkage and bronchiectasis in the involved part of the lung. The interval of time which is supposed to differentiate the two varieties is arbitrary and varies with different writers. It is usually given as six to 12 weeks. This clinical differentiation between the two varieties of abscess, on the basis of a time factor, puts one in the absurd position of having to say that an abscess changes from one type to the other overnight. It also necessitates the selection of a certain day for the beginning of every abscess, whereas in some instances the history of onset is so vague that it is impossible to determine with any accuracy when the abscess originated. Furthermore, even when the approximate time of onset is known, a time-interval alone, whether it be six weeks, eight weeks, or 12 weeks, is not a reliable criterion. There will always be some abscesses which drain poorly and become associated with fibrosis and bronchiectasis before the elapse of this time and others that drain well and remain uncomplicated for a longer period. Furthermore, there are probably other factors which determine the development of these complications, such as the type and virulence of the infecting agent and the resistance of the patient.

These are my reasons for disliking a clinical classification based on time. It is inaccurate. On the contrary, a classification based on pathology directs attention at once to the complications which are so frequently associated with pulmonary abscess and which have such an important influence on the outcome.

BACTERIOLOGY

In spite of extensive investigation the relative importance of different bacteria in the development of pulmonary abscess is still unknown. Clinically, however, two types of lung abscess *can* be distinguished. One of these, which is by far the more common, is associated with a very foul odor. The other is not. The odor is striking and can usually be recognized at the bedside, when the abscess discharges its contents through a bronchus, or in the operating room, when the abscess is opened surgically. This foul type of abscess is now generally believed to represent an anaerobic infection of the lungs, caused by organisms which are commonly found in dirty mouths. The anaerobes which are thought to be of greatest importance include the *Spirochaeta* and fusiform bacilli of Vincent, the *Bacterium melaninogenicum*, *Vibriones* and streptococci.

Some authors, notably Wessler¹ and Neuhoof,² believe that the odor is diagnostic and always represents an anaerobic infection. They also believe that the lesion produced represents a peculiar type of pathology which is characterized by mass tissue necrosis, or gangrene. This may be localized to a small area or spread to involve an entire lobe. Such lesions are called "gangrene of the lung" by Wessler and, when localized, "putrid lung abscess" by Neuhoof. Both of these authors distinguish them from the more rare "second type" of lung abscess which is not fetid and which is found in association with a wide variety of aerobic pyogenic bacteria.

In this report the fetid and nonfetid varieties of abscess are discussed separately because, in spite of the uncertainty as to the causal relationship of various bacteria, I also believe that an abscess which is fetid in its early stages represents an anaerobic infection of the lungs and presents a different problem in therapy than is presented by a nonfetid abscess. It was considered futile to attempt a bacteriologic classification when the exact part played by different bacteria is still uncertain. Furthermore, this would have been impossible, because complete bacteriologic studies, including darkfield examinations and anaerobic cultures, were not made in all of the cases, and most of the cases were of many months' standing when they first came under my observation. Obviously, the bacteria recovered from an abscess of many months' duration are not necessarily the same as those which initiated the process.

Even though the exact importance of anaerobic bacteria in the development of an abscess has not been established to the satisfaction of all, the results of the bacteriologic studies made on the patients with fetid abscess, which are included in this report, would certainly seem to be of some significance. In spite of the fact that complete studies were not made in all instances, either anaerobic streptococci, *Bacterium melaninogenicum*, *Vibriones*, *Spirochaeta* or fusiform bacilli, singly or in varying combinations, were recovered from the sputum, abscess contents, or empyema fluid in 42 of the 70 fetid cases in the series. The organisms recovered in the nonfetid cases included the Friedlander bacillus in one case, *Aspergillus fumigatus* in one, pneumococcus Type-III in one, hemolytic *Staphylococcus aureus* in one, and hemolytic streptococcus in two. Bacteriologic studies in the other two nonfetid cases were unsatisfactory.

PATHOGENESIS

There are several etiologic factors which are important both from the diagnostic and therapeutic standpoints. For instance, the history of onset in the majority of fetid abscesses suggests that they are due to the aspiration of infected material from the mouth. A great many are postoperative, and most of these occur after operations upon the upper respiratory tract, such as tonsillectomies, laryngectomies, tooth extractions and drainage of abscesses. Some of the cases that occur following other types of operations are clearly the result of secondarily infected infarcts. Not a few fetid abscesses occur

after periods of unconsciousness due to alcohol, drowning accidents, insulin shock, trauma, or epileptic seizures. In this group there is sometimes a definite history of the aspiration of vomitus, water, or some other foreign material. In contrast, the history of onset in most of the nonfetid abscesses suggests an embolic or postpneumonic origin. Both types occur, however, without a history of antecedent trauma, operative procedure, or pneumonia. Thus, it should be emphasized that, even if an etiologic factor predisposing to aspiration is absent, fetid abscesses are probably aspiration abscesses and represent infection either primary or secondary, caused by the group of anaerobic organisms mentioned above.

PATHOLOGY AND CLASSIFICATION

In its early stages a pulmonary abscess may be looked upon as a localized area of necrosis and suppuration which is unassociated with any significant amount of fibrosis and bronchiectasis. Of all the factors concerned in the healing of such a process free drainage is by far the most important. This may occur spontaneously through a bronchus or may be established by operation. In either event the result may be equally good. If free drainage is not obtained early, however, certain complications and permanent changes in the adjacent lung are likely to occur, both secondary to the persisting infection. The usual complications are a spreading pneumonitis, bronchopneumonia, secondary abscesses and empyema. The permanent changes in the adjacent lung are fibrosis and bronchiectasis. The presence of fibrosis and bronchiectasis is generally understood as establishing the difference between an acute and chronic process.

When a lung abscess is complicated by empyema or pyopneumothorax it usually means that the abscess has perforated into the pleural cavity and that a bronchopleural fistula exists (so-called pleuropulmonary abscess). This is not an uncommon complication of abscess and, in many instances, the fistula can be demonstrated, either at operation, or subsequently during the postoperative course. Empyema may also follow a diagnostic aspiration of a lung abscess from contamination of the pleural cavity by the needle. Since this does not seem to be an infrequent occurrence it is felt that a deliberate lung puncture should never be made in a case of suspected abscess, and that diagnostic punctures, in general, should be avoided whenever possible, for fear of accidental lung injury and pleural infection. The danger of infecting the pleural cavity by thoracentesis seems to be greater in the anaerobic infections. When empyema is a complication of a fetid abscess the exudate is foul and usually much thinner than the exudate which is seen in the more familiar pneumococcal and streptococcal varieties of empyema. Cultures reveal the same anaerobic organisms which are found in association with fetid abscesses. Empyemata similar to these, and associated with the same organisms, are occasionally seen when there is no evidence whatsoever of either a preceding or coexisting abscess. The origin of the empyema in cases of this kind is obscure. There is reason to believe that some foul

empyemata are caused by anaerobic streptococci alone. These cases appear to be postpneumonic and the exudate is thick, not unlike that seen in the pneumococcal and hemolytic streptococcal infections. Occasionally the presence of a lung abscess is never suspected until foul pus is aspirated from the pleural cavity. When empyema occurs as a complication of lung abscess it may be a small, well-encapsulated collection of pus, or a large, poorly circumscribed collection occupying the greater part of the pleural space. The smaller encapsulated forms are found, not infrequently, in one of the interlobar spaces, and I have the impression that they are seen especially in association with upper lobe abscesses. They suggest slow leakage from the underlying abscess, allowing time for protective adhesions to form. The massive types suggest sudden rupture into a virgin pleural cavity.

TREATMENT

Uncomplicated Abscess—Fetid Type—In common with Wessler, Neuhof, and many others, I feel that a fetid abscess is essentially a surgical disease. This is not meant to imply that all cases require operation. On the contrary, I believe that all cases should have a trial of conservative therapy, because some will drain freely through the bronchial tree and heal satisfactorily without surgical interference. The majority, however, do not, and for this reason, during the period of conservative treatment, the patients should be under the closest supervision of both the internist and the consulting surgeon. When evidence of free drainage and progressive healing becomes questionable, surgical drainage should be instituted at once, unless there is some very good reason for not doing so. *Early free drainage is essential to avoid the development of complications and the higher operative mortality and less satisfactory late results in the complicated cases.* Unfortunately, the medical profession, at large, does not seem to appreciate this, for in most clinics it is still true that the majority of cases are not referred for surgical treatment until after complications have developed. In the series of abscesses herewith reported, 54 out of 78, or 69 per cent, fell into this group.

Precise localization of the cavity is by far the most important technical factor in determining the success of the operation. When the abscess is situated in the peripheral part of a lobe, as most of them are, adhesions form early between the overlying visceral and parietal layers of pleura and make drainage of the abscess possible in a one-stage procedure without opening and infecting the pleural cavity. In some instances, however, adhesions are not found, either because the surgical approach is not correct or because the cavity is central and unassociated with pleural adhesions. Under these conditions the operation must be undertaken in two stages. At the first stage the wound is packed with iodoform gauze in order to produce the desired adhesions artificially. It is important to place the iodoform gauze in close contact with the parietal pleura. The abscess is opened six to eight days later. In the interval, roentgenologic studies to localize the cavity should be repeated. The number of operations that have to be divided into stages should

decrease as a surgeon becomes more proficient in localization. In general, upper and middle lobe abscesses are more directly drained through an anterior or axillary approach and lower lobe abscesses through a posterior approach. Local anesthesia is the anesthesia of choice in all cases.

Uncomplicated Abscess—Nonfetid Type—Early drainage is also of importance in this group although perhaps less so than in the fetid abscesses. This is because the associated aerobic bacteria are less destructive than the anaerobic bacteria found in the fetid cases and are less prone to cause secondary abscesses and empyema. On the other hand, early drainage to avoid secondary fibrosis appears to be equally as important. Nonfetid abscesses are relatively rare in comparison with fetid abscesses and are often unsuitable for operation because of their extent and the presence of other septic foci. The operative technic in these cases is the same as that in the fetid cases.

Complicated Abscess—Fetid and Nonfetid Types with Multiple Cavities—Multiple cavities may require drainage at two separate sites. When they involve the same bronchopulmonary segment, however, usually a single approach will suffice. If the "several cavities" prove to be one large multilocular cavity, and the smaller chambers drain freely into the main space, a simple unroofing operation of the main cavity may provide the necessary drainage. Otherwise, it may be necessary to unroof each cavity separately.

Complicated Abscess—Fetid and Nonfetid Types with Empyema—When an abscess is complicated by empyema, the empyema should be drained first. In most cases drainage of the empyema will suffice because the abscess drains freely into the empyema cavity at the site of rupture. In the fetid cases it is important to operate immediately because of the marked sepsis usually present in these infections and in order to avoid the development of a cellulitis of the chest wall from bacteria implanted in the needle tract at the time of thoracentesis. When the empyema is small and well-encapsulated, drainage should be instituted through a large opening into the dependent part of the cavity. When, on the other hand, the empyema cavity is large and poorly circumscribed, an open thoracotomy may be hazardous. In cases of this kind the opening into the pleural cavity should be large, but measures should be taken to prevent a "sucking" wound until the desired adhesions have formed. If there is a fistula, continuous suction might help in preventing the aspiration of exudate from the empyema cavity, with spread of infection to other bronchi. Swabbing or irrigating the cavity with an aqueous solution of gentian violet seems to help in some cases. Whether this is due to the prevention of secondary infection or to a specific effect of the gentian violet on the organisms which were primarily responsible for the abscess is not clear. When there is no fistula other antiseptics such as Dakin's solution or zinc peroxide may be used. When improvement does not follow drainage of the empyema, inadequate drainage of the underlying abscess should be suspected. Other likely causes are pulmonary gangrene, suppurative mediastinitis and brain abscess. Empyema is rarely seen in association with a proved nonfetid abscess. It did not occur once in the eight cases of nonfetid abscess.

included in this report, whereas the instance of empyema in the fetid cases was 23 per cent

Complicated Abscess—Fetid and Nonfetid Types with Notable Fibrosis and Bronchiectasis—The treatment of lung abscess with secondary fibrosis and bronchiectasis is the same, regardless of whether the preceding abscess was fetid or nonfetid. Conservative measures will not produce healing in cases of this kind. Surgery offers the only hope of cure and, here again, the first consideration should be efficient drainage of the involved part of the lung. The rationale for this is twofold. In the first place, occasionally such a case will heal after free drainage is established, and in the second place, those that do not heal are improved by drainage and hence become better risks for what further procedures are indicated. If there is a minimal amount of bronchiectasis, satisfactory drainage can often be obtained by simply unroofing the cavity. On the other hand, when there is advanced bronchiectasis efficient drainage can only be established by destroying some of the involved part of the lung. The cautery is the best means for accomplishing this.³ Both the electric and actual cauteries can be used. Experience seems to have shown, however, that the latter is less likely to be associated with hemorrhage and air embolism and is, therefore, preferable. The use of the cautery to secure drainage is best suited to peripheral lesions that involve only one lobe of a lung. When a large part or all of a lobe is involved the amount of lung tissue which must be destroyed in order to obtain satisfactory drainage is so large that spontaneous healing seldom follows. The result may be a single fistula, but in most instances it will be a residual cavity in the lung itself with multiple bronchial communications. Fibrous partitions of varying height divide the walls of such a cavity into recesses which, in time, may become completely covered by epithelium. Patients with pathology such as this are often in the best of health except for their fistulae. Another surgical procedure is necessary, however, in order to produce healing. This should be a plastic operation, with excision of the mucous membrane lining the cavity and closure of the fistulae if the central part of the lobe is normal.⁴ Lobectomy is the better procedure when the remnant of cauterized lobe is fibrotic and bronchiectatic.

When fibrosis and bronchiectasis involves more than one lobe, cautery pneumonectomy is less practical. In cases of this kind immediate removal of all of the diseased part of the lung is the only rational procedure. This may require a bilobar lobectomy, or total pneumonectomy. It should be realized, however, that the mortality of such procedures is high, especially so in the presence of residual pus in patients with fever, leukocytosis, debility, cyanosis and copious amounts of sputum. The use of suction to remove exudate from the trachea and bronchi before, during, and immediately after operation upon patients of this kind is of great importance.

CLINICAL MATERIAL

This report is based on the records of 78 consecutive patients who were treated surgically at the Presbyterian Hospital during the past 11 years.

Fifty-one were males, 27 were females. Of the 78 patients, only 24 had uncomplicated abscesses at the time surgery was instituted, leaving 54 patients who had already developed complications. In the uncomplicated group, 23 of the cases were fetid, and 1 was nonfetid. In the complicated group, 47 of the cases were fetid and 7 were nonfetid. Of the 47 patients with fetid abscess and complications, 14 had multiple cavities, 16 had empyema, 2 notable fibrosis of the lung, 13 bronchiectasis, 1 a mediastinal abscess, and 1 an abscess of the kidney. All of the patients with nonfetid abscess and complications had extensive fibrosis of the lung (Table I).

TABLE I

CLINICAL MATERIAL

Seventy-eight Patients with Pulmonary Abscess

I	Uncomplicated		24
	A	Fetid	23
	B	Nonfetid	1
II	Complicated		54
	A	Fetid	47
		Multiple cavities	14
		Empyema	16
		Notable fibrosis	2
		Bronchiectasis	13
		Mediastinal abscess	1
		Abscess of the kidney	1
	B	Nonfetid	7
		Multiple cavities	0
		Empyema	0
		Notable fibrosis	7
		Bronchiectasis	0

When the patients were grouped according to duration of symptoms it was found that only 31 had had symptoms for less than 2 months at the time of operation. Of these, 18, or 58 per cent, had already developed complications. The 18 included 4 patients with multiple cavities, 13 with empyema, and 1 with bronchiectasis. When the interval of time was extended to 3 months the percentage of complicated cases was the same. There were 40 patients in this group, 6 of whom had multiple cavities, 14 empyema, 1 notable fibrosis, 1 bronchiectasis, and 1 a mediastinal abscess. After this, the percentage of patients with complications increased with the duration of symptoms but the type of complication changed. When the duration of symptoms exceeded 3 months (38 patients), 31, or 82 per cent, had complications. In this group, however, there were only 2 cases with empyema. Eight of the others had multiple cavities, 8 notable fibrosis, 12 bronchiectasis, and 1 a sinus extending through the diaphragm into an abscess of the kidney (Table II).

RESULTS

Uncomplicated Abscess—Fetid Type—Of the 23 patients with uncomplicated abscess of the fetid type 21 recovered. All of these are still alive and have been followed for periods of time varying from a few months to 11 years. Nineteen have healed wounds and are free of symptoms. Two are healed, with a residual cough. The mortality in this group (2 deaths) was

PULMONARY ABSCESS

TABLE II
CLINICAL MATERIAL

Seventy eight Patients with Pulmonary Abscess

1	With symptoms not exceeding 2 months		31
	Uncomplicated	13	
	Complicated	18 (58%)	
	Multiple cavities	4	
	Empyema	13	
	Bronchiectasis	1	
2	With symptoms not exceeding 3 months		40
	Uncomplicated	17	
	Complicated	23 (58%)	
	Multiple cavities	6	
	Empyema	14	
	Notable fibrosis	1	
	Bronchiectasis	1	
	Mediastinal abscess	1	
3	With symptoms for more than 3 months		38
	Uncomplicated	7	
	Complicated	31 (82%)	
	Multiple cavities	8	
	Empyema	2	
	Notable fibrosis	8	
	Bronchiectasis	12	
	Abscess of kidney	1	

9 per cent One patient died on the fifth day from a pneumonia, which appeared to be due to the aspiration of exudate which spilled into the air passages either during or soon after the operative procedure The other death was apparently caused by an acute agranulocytosis This patient, a male diabetic, age 58, had a large abscess of the middle lobe He was treated vigorously with sulfapyridine before transfer for surgery, and at the time of operation had a leukopenia At operation, a large piece of sequestered lung tissue was removed from the abscess cavity The agranulocytosis developed immediately after operation The patient ran a high temperature, showed no tendency to improve, and died on the fourth postoperative day The results are summarized in Table III, and the surgical procedures are given in Table IV

TABLE III
UNCOMPLICATED FETID ABSCESS

Mortality and Late Results in 23 Consecutive Patients

Recovered	21
Healed and symptom-free	19
Followed 0-2 years	9
Followed 2-4 years	4
Followed 4-6 years	5
Followed 10 years 9 months	1
Healed, with slight symptoms remaining	2
Followed 3 years 6 months	1
Followed 9 years 1 month	1
Mortality—9%	

Uncomplicated Abscess—Nonfetid Type—Bacteriologic study of the exudate taken from the abscess cavity at the time of operation, in the one patient who had an uncomplicated abscess of the nonfetid type, revealed a pure

TABLE IV

UNCOMPLICATED FETID ABSCESS

Surgical Procedures in 23 Consecutive Patients

Rib resection and drainage in 1 stage	14
Rib resection and drainage in 1 stage followed by closure of fistula	1
Rib resection and drainage, in 2 or more stages	8

culture of Friedlander bacillus This abscess was drained in two stages The patient made an uneventful recovery, and was completely relieved of symptoms Follow-up observations continued until his death from carcinoma of the esophagus, six and one-half years later

Complicated Abscess—Fetid Type, with Multiple Cavities—In this group there were 14 patients Of these, 9 recovered, and have been followed for periods of time varying between 9 months and 7 years Five of the 9 have healed wounds, and are symptom-free, one has a residual cavity, with fistulae, one is healed, with slight symptoms, one still has a bronchocutaneous fistula after two and one-half years, and the other, also with a bronchocutaneous fistula, died of a streptococcal wound infection and septicemia following appendectomy, 22 months after the surgical attack on the abscess was completed The mortality in this group (5 deaths) was 36 per cent One patient died during operation, death apparently being related to the administration of the anesthetic Another died of a massive hemorrhage from the lung, two and one-half years after drainage of a large middle lobe abscess Another, a male diabetic, age 59, died of unknown cause a few weeks after discharge from the hospital The other two died of pneumonia, 1 eight days after operation, and the other two years after operation The results are summarized in Table V, and the surgical procedures in Table VI

TABLE V

COMPLICATED ABSCESS—FETID TYPE WITH MULTIPLE CAVITIES

Mortality and Late Results in 14 Patients

Recovered	9
Healed and symptom free	5
Followed 9 months	1
Followed 1-2 years	2
Followed 2 years 4 months	1
Followed 7 years 4 months	1
Residual cavity with fistulae	1
Followed 1 year 6 months	
Healed with slight symptoms remaining	1
Followed 1 year 9 months	
Bronchocutaneous fistula	2
Followed 1 year 10 months	1
Followed 2 years 6 months	1
Mortality—36%	

TABLE VI

COMPLICATED ABSCESS—FETID TYPE WITH MULTIPLE CAVITIES

Surgical Procedures in 14 Patients

Rib resection and drainage in 1 or more stages	6
Rib resection and drainage followed by lobectomy	1
Cautery pneumonectomy in stages	4
Cautery pneumonectomy followed by closure of fistula	1
Cautery pneumonectomy followed by unsuccessful closure of fistula	1
Pneumonectomy attempted but not completed	1

Complicated Abscess—Fetid Type, with Empyema—Seventeen of the patients with fetid abscesses had an associated empyema or pyopneumothorax. One of these, with symptoms of more than a year's duration, had, in addition, extensive fibrosis and bronchiectasis of the involved lung, and is included in the group with these complications. Of the remaining 16 patients, 11 recovered, and all of these have been followed to the present time. Ten of the 11 have healed wounds, and are symptom-free, and 1 has a bronchocutaneous fistula. The mortality (5 deaths) was 31 per cent. Two of the patients who died developed brain abscesses. Another developed an extensive necrotizing cellulitis of the chest wall and lumbar region. A fourth developed large areas of gangrene in both lower lobes. The fifth death, which came suddenly on the fourth day after operation, was apparently caused either by a massive cardiac infarction or pulmonary embolism. The duration of symptoms previous to operation was less than six weeks in ten of the patients. The results are shown in Table VII, and the surgical procedures in Table VIII.

TABLE VII
COMPLICATED ABSCESS—FETID TYPE WITH EMPYEMA
Mortality and Late Results in 16 Consecutive Patients

Recovered	11
Healed, and symptom-free	10
Followed 0-1 year	2
Followed 1-2 years	4
Followed 2-3 years	2
Followed 3 years 6 months	1
Followed 4 years 4 months	1
Bronchocutaneous fistula	1
Followed 7 months	
Mortality—31%	

TABLE VIII
COMPLICATED ABSCESS—FETID TYPE WITH EMPYEMA
Surgical Procedures in 16 Consecutive Patients

Rib resection, with drainage of empyema only	14
Rib resection with drainage of empyema followed by drainage of abscess	2

Complicated Abscess—Fetid Type, with Fibrosis of the Lung and Bronchiectasis—In this group there were 15 patients, 13 with proved bronchiectasis, and two with fibrotic lobes, without demonstrable bronchiectasis cavities. Only 1 of the 15 patients had had symptoms for less than three months. In 8, the duration of symptoms exceeded one year, and in the other 6, symptoms had been present for periods of time varying between four and ten months. In reporting results, the two patients with pulmonary fibrosis, but without demonstrable bronchiectasis, have been grouped with the 13 with bronchiectasis because of my belief that these two conditions rarely, if ever, occur separately in fetid cases of pulmonary suppuration. Ten of the patients recovered, and all of these have been followed for varying periods of time. Only four have healed wounds and are symptom-free. Two are healed, with slight symptoms. Four have bronchocutaneous fistulae. The mortality

(5 deaths) was 33 per cent. Three of the deaths were apparently caused by a postoperative pneumonia, resulting from the aspiration of exudate which spilled into the air passages either during or soon after the operative procedure. One death was due to a severe hemorrhage, which occurred during operation, when the stump of an amputated lobe slipped out of the lobectomy cord. The other patient died on the fifth postoperative day of extensive infection including secondary abscesses in the opposite lung, a severe purulent bronchitis and empyema. Results are shown in Table IX, and operative procedures in Table X.

TABLE IX

COMPLICATED ABSCESS—FETID TYPE WITH FIBROSIS AND BRONCHIECTASIS
Mortality and Late Results in 15 Patients

Recovered	10
Healed and symptom free	4
Followed 2 years 9 months	1
Followed 4 years 7 months	1
Followed 6 years 6 months	1
Followed 8 years 5 months	1
Healed with slight symptoms remaining	2
Followed 5 years 8 months	1
Followed 5 years 9 months	1
Bronchocutaneous fistula	4
Followed 4 months	2
Followed 1 year 8 months	1
Followed 5 years 9 months	1

Mortality—33%

TABLE X

COMPLICATED ABSCESS—FETID TYPE WITH FIBROSIS AND BRONCHIECTASIS
Surgical Procedures in 15 Patients

Rib resection and drainage in 1 or more stages	3
Rib resection and drainage followed by closure of fistula	1
Cautery pneumonectomy in stages	4
Cautery pneumonectomy followed by lobectomy	6
Primary lobectomy	1

Complicated Abscess—Nonfetid Type, with Notable Fibrosis of the Lung—There were seven patients in this group, and all had had symptoms for months or years before the surgical attack was begun. Six recovered, and have been followed for varying periods of time. Four of these have healed wounds, and are symptom-free. Two have open wounds, with residual cavities in the lung and multiple fistulae. The one death occurred on the fifth day postoperative from coronary thrombosis. Mortality and late results are summarized in Table XI, and surgical procedures are given in Table XII.

TABLE XI

COMPLICATED ABSCESS—NONFETID TYPE WITH FIBROSIS
Mortality and Late Results in 7 Patients

Recovered	6
Healed and symptom free	4
Followed 5 months	1
Followed 5-6 years	3
Open wounds with residual cavity and fistulae	2
Followed 2 years 2 months	1
Followed 4 years	1

Mortality (1 death)—14%

TABLE XII

COMPLICATED ABSCESS—NONFETID TYPE WITH FIBROSIS AND BRONCHIECTASIS

Surgical Procedures in 7 Patients

Rib resection and drainage in 1 stage	4
Rib resection and drainage followed by closure of fistula	1
Rib resection and drainage followed by lobectomy	1
Primary lobectomy	1

All Cases—Uncomplicated and Complicated—Of the 78 patients operated upon, 43, or 55.1 per cent, are apparently cured, *i e*, they have healed wounds, and are entirely free of symptoms, 10, or 12.8 per cent, have bronchial fistulae, 5, or 6.4 per cent, have healed wounds, with persistent cough and sputum, and 20, or 25.7 per cent, are dead. The results were not tabulated according to procedure because of the great variation in the extent of the pathologic processes in the different patients, and the small number of patients in any particular group. None of the patients were exactly alike, and none of them with the same complications presented the same operative risk.

SUMMARY

(1) The bacteriology, pathogenesis, pathology and treatment of pulmonary abscess are discussed, and the records of 78 patients who were treated surgically by the author were reviewed. The cases were classified as *uncomplicated* or *complicated*, according to pathology, and as *fetid* or *nonfetid*, according to odor. By definition, a case was considered *uncomplicated* when there was only one abscess, and this was unassociated with empyema, notable fibrosis of the lung, bronchiectasis, or other serious complications. Cases with multiple abscess, empyema, notable fibrosis, bronchiectasis, or other latent complications such as suppurative pericarditis and suppurative mediastinitis were classified as *complicated*. The criteria for classification are given in detail. The common practice of describing abscesses as "acute" and "chronic," according to duration, is condemned because the terms *acute* and *chronic* do not have exact meanings, and have led to much confusion.

(2) Of the 78 patients, only 24 had uncomplicated abscesses. Of the 54 with complications, 16 had empyema, 14 multiple cavities, 13 bronchiectasis, 9 notable fibrosis of the lung, 1 a mediastinal abscess, and 1 an abscess of the kidney. In the uncomplicated group, 23 of the cases were fetid, and 1 was nonfetid. In the complicated group, 47 of the cases were fetid, and 7 were nonfetid. Fifty-eight per cent of the patients who had had symptoms for less than three months, at the time of operation, were complicated, and 82 per cent of the patients who had had symptoms for more than three months, were complicated. In the fetid group, empyema and multiple abscesses were frequently seen in the early stages, whereas fibrosis and bronchiectasis, with or without secondary abscesses and empyema, were regularly seen in the cases of many months' standing. In the nonfetid group none of the cases had empyema or bronchiectasis, but all of the cases of long standing had unmistakable evidence of extensive pulmonary fibrosis.

(3) Of the 24 patients with uncomplicated abscess, only 2 died, an operative mortality of 8 per cent. In contrast, the operative mortality in the 54

patients with complications (18 deaths) was 33 per cent. In this latter group, composed largely of fetid cases, the mortality in the fetid cases with multiple cavities was 36 per cent, in the fetid cases with empyema it was 31 per cent, and in the fetid cases with fibrosis and bronchiectasis it was 33 per cent. In the nonfetid cases, all of whom had extensive pulmonary fibrosis, and none of whom had empyema or bronchiectasis, it was 14 per cent (1 death). The surgical procedures are given.

(4) All of the survivors were followed for periods of time varying from a few months to 11 years. The late results were better in the uncomplicated group and in the fetid group that was complicated by empyema. In the former, 91 per cent of the patients had healed wounds, and were free of symptoms. In the latter, 90 per cent of the patients fell into this category. In contrast to these figures, only 52 per cent of the patients that had multiple abscesses, extensive fibrosis or bronchiectasis were free of symptoms. In this group, 3 patients still had open wounds, with residual cavities in the lung and multiple fistulae, 3 others, although healed, still had symptoms, and 6 others had bronchocutaneous fistulae. All of the cases that were complicated by empyema alone, were of short duration, and the excellent final results in this group were no doubt due to early rupture of the abscess and free drainage into the pleural cavity.

CONCLUSIONS

(1) Early, free drainage of a pulmonary abscess is essential in both the fetid and nonfetid types to avoid the development of complications, the higher operative mortality, and the less satisfactory late results in the complicated cases. For this reason, pulmonary abscess, especially the fetid type, should be accepted as a surgical disease and should be treated under the direction of a surgeon.

(2) The division of cases into "acute" and "chronic," on the basis of time, is confusing. Cases should be classified on the basis of pathology.

(3) A pathologic classification is essential for selecting the proper surgical procedure, and is the most reliable basis for estimating operative risk and late prognosis. It is also important for purposes of comparison between different series of reported cases.

REFERENCES

- ¹ Wessler, H. Abscess and Gangrene of the Lungs, Diseases of the Respiratory Tract. Eighth Annual Graduate Fortnight of the New York Academy of Medicine. Philadelphia, Pa., W. B. Saunders Co., p. 295, 1936.
- ² Neuhoof, H., and Touroff, A. S. W. Acute Putrid Abscess of the Lung—A Surgical Disease. New York State Jour. Med., 40, 849, No. 11, 1940.
- ³ Graham, E. A. Pneumectomy with Cautery—A Safer Substitute for the Ordinary Lobectomy in Cases of Chronic Suppuration of the Lung. J. A. M. A., 81, 1010, 1923. Idem. Cautery Pneumectomy for Chronic Suppuration of the Lung. Report of 20 Cases. Arch. Surg., 10, 392, 1925.
- ⁴ Lebsche. Cited from Sauerbruch (Sauerbruch, E. Die Chirurgie der Brustorgane. Berlin, Ed. 3, 1, 900, Julius Springer, 1928).

CONTROL OF MASSIVE ESOPHAGEAL HEMORRHAGE SECONDARY TO LIVER DAMAGE (CIRRHOSIS) BY LIGATION OF THE CORONARY VEIN AND INJECTION OF SODIUM MORRHUATE

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THE CLINICAL ENTITY of cirrhosis of the liver is relatively constant, in general, but reveals many different causes and many secondary complications. Among the latter, esophageal hemorrhage is frequent and often so severe that death may follow. With our increasing knowledge of liver function, many so-called hopeless cases of liver damage might be helped by using all known data now available for the preservation and restoration of liver function.

The liver is not only the largest but one of the most vital organs in the body, and in spite of its multiplicity of functions the two considered most important are: First, its ability to function with a small amount of normal tissue, and, second, its remarkable capacity to regenerate. Since the causative element in liver damage may in many instances be one not classically accepted or known, every aid should, therefore, be given such patients in spite of the apparently hopeless picture. The multiple functions of the liver make it easy to appreciate the fact that, when this organ is badly damaged, any complication may precipitate a fatality.

Varices, one of the more common complications of the cirrhotic liver, are caused by a greater flow of blood through a vein and by the inability of the muscular and elastic fibers to prevent this increased venous pressure. Since the submucous veins of the esophagus are well supported at the cardia, the formation of varices probably occurs below the cardia and spreads above that point after anastomosis has been completed. The formation of varices above the cardia is undoubtedly more rapid when several large veins cross the cardia. These are probably the first veins in the cardiac region to become enlarged.⁴

Unlike the obstruction of the portal or splenic vein in Banti's disease and splenic anemia, the physiologic changes involved in the occurrence of esophageal varices may have an intrinsic or extrinsic cause. When the portal or splenic vein is obstructed anastomosis results, in order that the blood from the portal circulation can pass back into the general systemic circulation. Doctor Moersch⁷ lists three existing routes through which this may take place, depending upon the site of the obstruction in the splenic or portal vein.

1. At the point of transition between absorbing and protective epithelium
 - (a) Between the coronary vein of the stomach and the intercostal, the azygos and the diaphragmatic veins.

- (b) The superior hemorrhoidal with the middle and inferior hemorrhoidal veins
- 2 Site of embryologic circulation—falciform ligament containing the para-umbilical veins
- 3 At all situations within the abdomen where the gastro-intestinal tract, its appendages or glands developed from it become retroperitoneal, developmentally, or adherent to the abdominal wall, pathologically

The first of these is of the most concern, since esophageal varices result from such a communication. This passageway between the coronary vein of the stomach and the azygos, intercostal, and diaphragmatic veins is undoubtedly the most likely to develop, since it is the most direct route between the portal and general systemic circulations. Moreover, as Doctor Moersch points out, the pressure within the portal circulation is increased, when the portal vein is obstructed, with a resultant reversal of the flow of blood through the coronary vein, partly due, no doubt, to the absence of valves. This reversal of the coronary blood flow, in turn, exerts pressure on the esophageal plexus, with the effectual formation of esophageal varices. Anastomosis between the portal and caval circulations takes place within the plexus formed by the branches of the coronary vein after reaching the submucosa of the cardia by way of piercing the muscular coats. Since the veins in the submucosa of the lower esophagus are not very well supported by connective tissue, the increased flow of blood through the vein plus the inability of the venous walls to withstand such pressure, causes varicose veins of the esophagus. Doctor Moersch also points out that the effect of the changing suction in the thoracic cage, due to respiration, must also be considered. Although esophageal varices may involve the greater part of the esophagus, it is usually limited to the lower one-third.

The difficulty of early diagnosis has always been a problem in cases of esophageal varices. Little progress was made in such diagnosis from 1839, when Powers gave the first report of varicose veins of the esophagus to medical literature, until 1925, when Jackson and his associates suggested the value of esophagoscopy. In 1928, Wolf described the roentgenologic technic in diagnosis and, in 1931, Kirklin and Moersch⁷ combined roentgenoscopic and esophagoscopic diagnostic technic. The fear of fatal hemorrhage, however, has curtailed the use of esophagoscopy to a certain extent.

For the prevention and control of such hemorrhage, several procedures have been followed at one time or another. Doctor Moersch⁷ lists such palliative measures as "Dietary restrictions, the use of local applications to the varix (diathermy, local compression, *etc*), injection of solutions into the general circulation to stimulate coagulation, and venesection, as suggested by Drenckhahn, to increase the viscosity of the blood."

Splenectomy has been performed most frequently in an attempt to prevent hemorrhage in the esophageal varices. This evidently decreases by 20 per cent the amount of blood passing through the portal circulation. By splenectomy, also, one source of anastomosis between the portal and caval

circulations is stopped by the severing of the vessels which run through the vasa brevia and which communicate with the esophageal veins. Splenectomy is sometimes followed by an omentopexy with the Talma-Morison operation to divert blood from the direction of the esophageal varices by means of an anastomosis between the portal and systemic circulations. The Eck fistula has also been recommended as one of the simplest methods of remedying varices.⁵

The ligation of the coronary vein to prevent hemorrhage in esophageal varices was first advocated and successfully tried in 1929 by Rowntree, Walters, and McIndoe. Such ligation was carried out to interrupt the flow of blood to the collateral veins in the lower end of the esophagus. This procedure, however, did not preclude all possibility of hemorrhage. In 1933, Kegaries³ recommended the ligation of the vasa brevia in addition to ligation of the coronary vein in order to prevent the formation of such varices when splenectomy was considered too dangerous. He suggested that mass ligation was possible and that relief from hemorrhage could be obtained by sectioning these veins in the course of splenectomy.

Although injections directly into the esophageal veins have been used as early as 1914, when normal horse serum was recommended by Jackson, Tucker, Cleif, Lukens, and Moore² for hemorrhage from ruptured varicose veins of the esophagus, it was not until 1933 that injections of a non-irritating yet sclerosing solution into the periesophageal or paraesophageal plexus (a method similar to that of obliterating varicose veins of the leg) at the same time as ligation of the coronary vein was suggested by Walters.¹⁰ About the same time, Moersch and Pemberton⁶ suggested the possibility of injecting a sclerosing solution into the esophageal varices by means of an esophagoscope. Failure to produce esophageal veins in dogs in order to experiment with this new method before attempting such treatment upon the human patient caused the idea to be unadaptable for the moment. In 1939 this method of treatment, the solution being quinine-uretan, was successfully carried out upon the human patient by Fiencknei and Crafoord,¹ of Stockholm. Moersch immediately duplicated the procedure with, thus far, successful results.

Nothing is more unpredictable than the favorable clinical results often obtained in spite of extensive liver damage. Modern therapeutic aid has further equipped the clinician. The case here reported represents one of advanced liver damage with ascites and esophageal varices, the latter ruptured, producing severe massive hemorrhage. An apparent hepatic fatality was avoided and the patient restored to improved health by combining ligation of the coronary vein with injection of sodium morrhuate. The patient is now enjoying good health and has no complaints, the hemoglobin is 96 per cent, no ascites are present. A splenectomy was not undertaken on this patient because it was doubted whether such an operation with its definitely higher operative mortality should always be undertaken.

Case Report—R. T., white, male, age 53, was admitted to the Kings County Hospital in October, 1938, with a classical clinical picture of cirrhosis of the liver, the

patient was cachectic, pale, and cadaverous-looking, with a large abdomen containing fluid and considerable weight-loss. He had had a massive acute hemorrhage from a ruptured esophageal varix. The past history showed that this was his fourth hospital admission for apparently the same complaint, and that he had been constantly subjected,

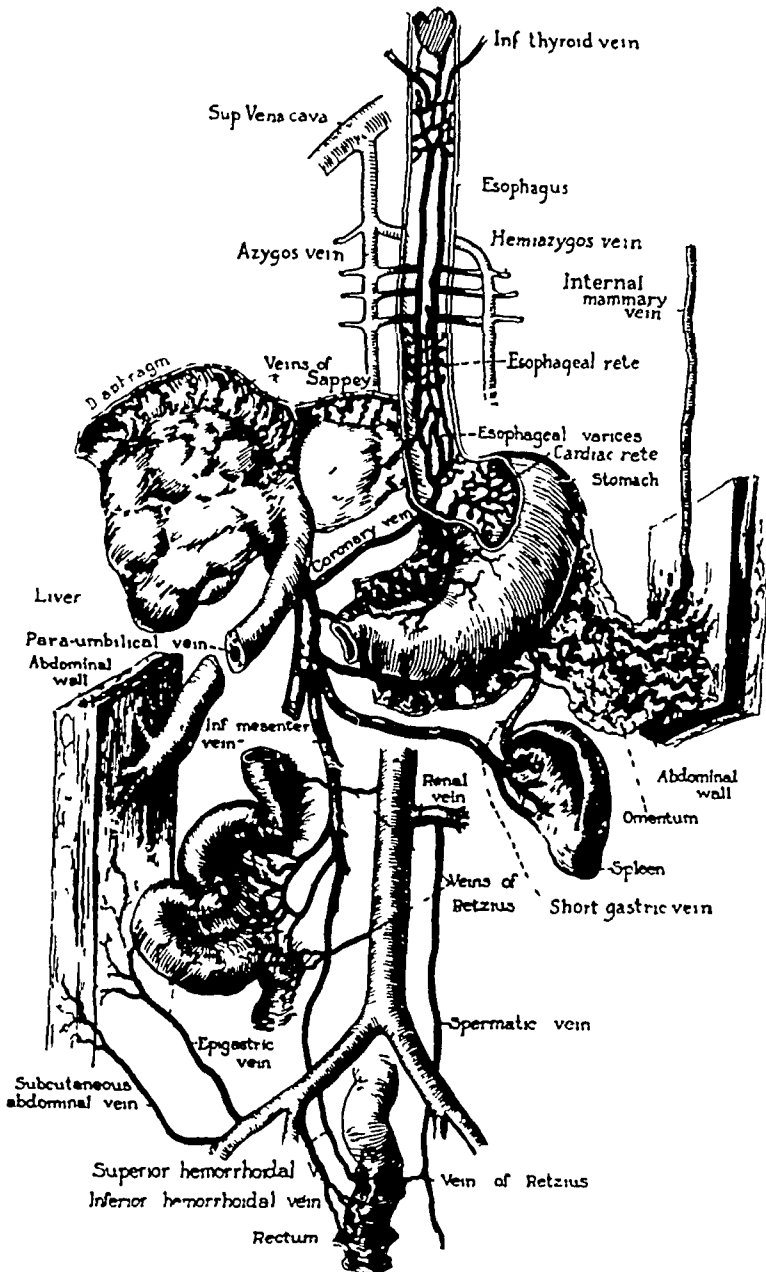


FIG 1—Diagrammatic study of the portal circulation with hepatic obstruction showing the anatomic reason for operative procedures described i.e., ligation of veins of Sappey, ligation and injection with sclerosive solution (sodium morrhuate) of the coronary vein and omentopexy (Talmi operation)

over a period of months, to these massive hemorrhages. The hemoglobin was 24 per cent, red count was 1,200,000. During his preoperative period, it was difficult on many occasions to obtain a pulse and blood pressure reading. Several small blood transfusions were given preoperatively with very slight clinical improvement.

In November a celiotomy was performed under a local anesthetic, and when the peritoneum was opened, a large quantity of ascitic fluid gushed forth. The coronary



FIG 2—Photomicrograph of a specimen of liver removed by biopsy at the time of celiotomy, showing cloudy swelling ($\times 159$)

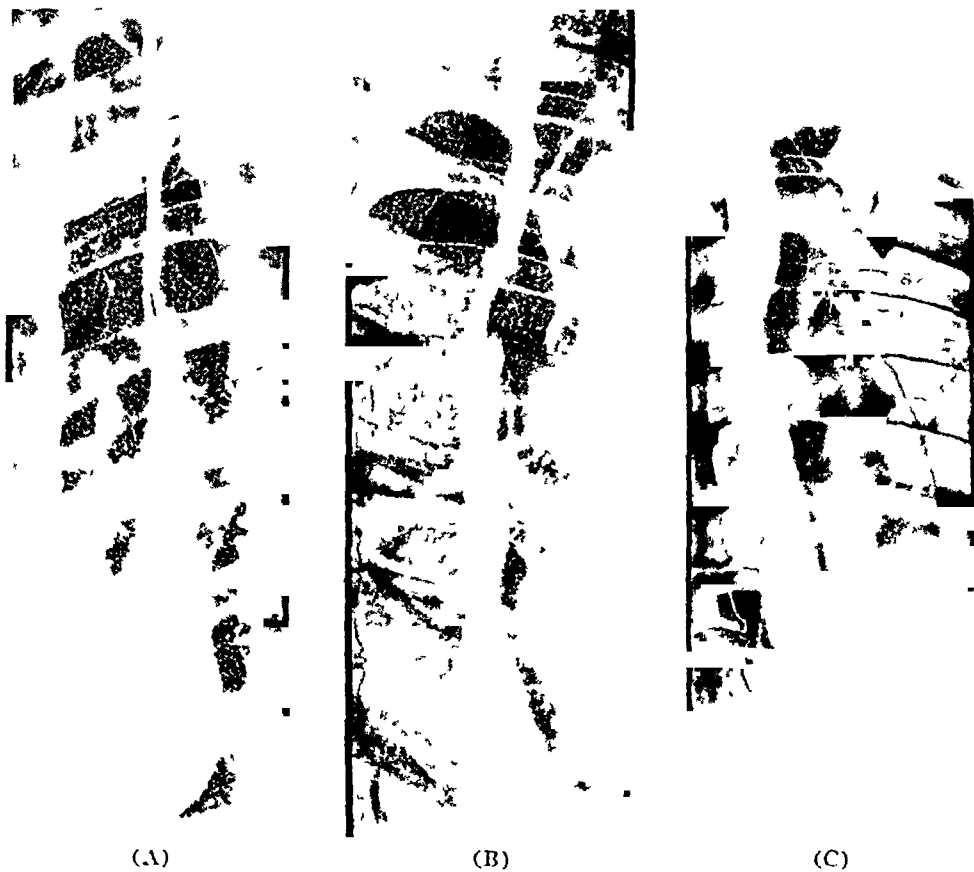
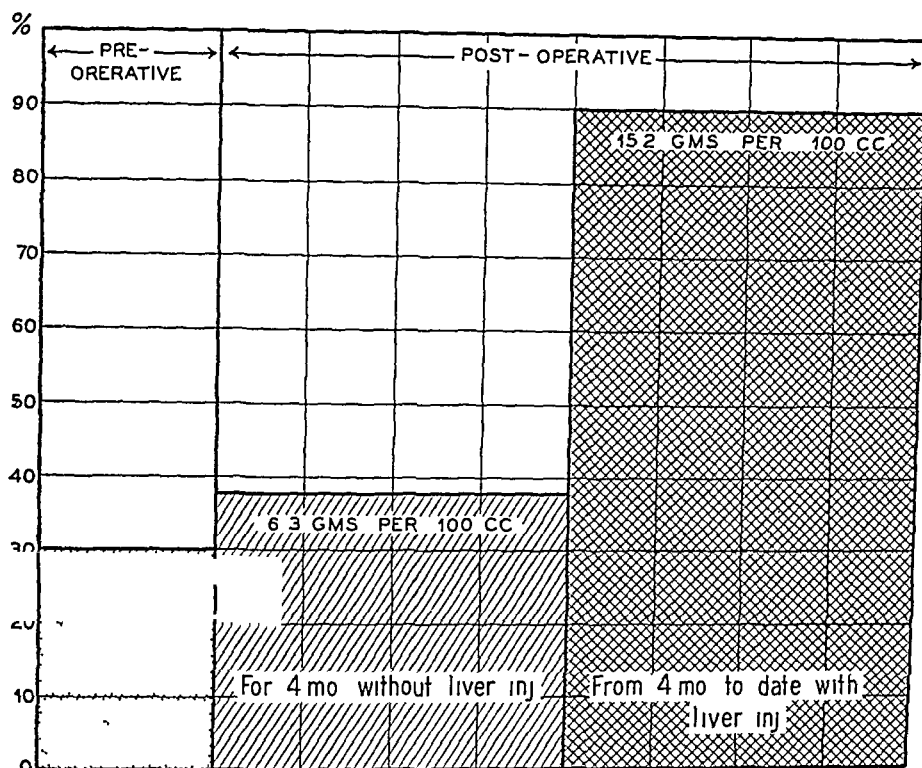


FIG 3—Drawings from esophagograms taken (A) Preoperatively (B) Four months postoperatively (C) Twenty months postoperatively

vein was found to be enlarged and distended (one centimeter in diameter), it was ligated with black silk, and eight cubic centimeters of sodium morrhuate solution was injected. Three other smaller veins, close to the coronary vein, were also ligated. It is interesting to note that after the above ligations, the veins between the ligature and the liver remained distended, while between the ligature and the esophagus they were collapsed. The veins of Sappey on the undersurface of the diaphragm were also ligated. In view of the above-mentioned collapse of the coronary veins, I did not feel that in this patient the danger of collateral circulation from the spleen was any immediate problem and consequently did not feel that a splenectomy was justifiable. Exploration of this organ showed it to be firmly adherent and bound down,

CHART I



HEMOGLOBIN STUDIES ON RUPTURED ESOPHAGEAL VARICES
Hemoglobin studies made on June 23, 1941 were 15.2 grams, or 102 per cent

apparently from an old perisplenitis. The liver was round-edged, pale yellow, and cirrhotic. A biopsy obtained from the liver edge subsequently confirmed the diagnosis of liver damage, however, the specimen was not predominantly fibrotic (Fig 2). About a month after the first operation, omentopexy was performed (Talma-Morison operation). After this last operation, a mild hemorrhage occurred at two different times, but since then, the patient, when recently seen, appeared to be in excellent health, had had no further hemorrhage and no evidence of ascites. In June, 1940, the hemoglobin had improved from 24 per cent, or four grams, to 80 per cent, or 12 grams. In November, 1940, the hemoglobin had further improved to 96 per cent, or 14.5 grams, according to the photo-electric cell method (Chart I). The liver function test was Grade O, with the serum bilirubin 1.5 mg per cent.

Roentgenologic studies made preoperatively showed evidence of esophageal varices, when these studies were repeated two months postoperatively, the esophagogram showed alterations indicative of improvement, and similar films taken six months after the ligation and injection of the veins showed a normal esophagus. Although clinical improvement has been marked, roentgenologic studies on August 3, 1939, and at the present

time, show some deviation from the normal, and the general appearance suggests a reversion back to the appearance of the roentgenogram taken preoperatively (Fig 3) The operation was, of course, directed at a complication of the liver damage (hemorrhage) and only indirectly could benefit accrue to the liver Although I appreciate fully the limitations of the liver function tests, it is interesting to note that on February 8, and on September 11, 1939, the bromsulfalein showed no dye retention This, with clinical improvement, is significant Furthermore, with the control of the massive hemorrhage and the use of all accepted modes of therapy for improving liver damage, such as a diet high in carbohydrates and low in fats, liver extract injections, and especially assimilation of vitamin B, which helps to restore liver function and speeds regeneration of the liver, I feel that these benefits should not be underestimated

Recent follow-up of this patient, May 15, 1942, finds him in excellent health and working daily running an elevator in a large apartment house

Liver injections for the past two years have been very irregular, averaging one a month, because of the difficulty the patient has in leaving his work

REFERENCES

- ¹Crafoord, Clarence, and Frenckner, Paul New Surgical Treatment of Varicose Veins of the Esophagus *Acta oto-laryng*, 27, 422-429, July-August, 1939
- ²Jackson, Tucker, Clerf, Lukens, and Moore Hematemesis *Laryngoscope*, 24, 154, 1914
- ³Kegaries, D L The Venous Plexus of the Esophagus *Proc Staff Meet, Mayo Clin*, 8, 160, March 15, 1933
- ⁴*Idem* The Venous Plexus of the Esophagus *Surg Gynec and Obst*, 58, 46, January, 1934
- ⁵McIndoe, A H Vascular Lesions of Portal Cirrhosis *Arch Path*, 5, 23, January, 1928
- ⁶Moersch, H J Treatment of Esophageal Varices by Injection *Proc Staff Meet, Mayo Clin*, 15, 177-179, March 20, 1940
- ⁷*Idem* Treatment of Esophageal Varices by Injection of a Sclerosing Solution (paper read before the meeting of the American Association for Thoracic Surgery, Cleveland, Ohio, June 6-8, 1940)
- ⁸Rowntree, L G, Walters, W, and McIndoe, A H A New Procedure in Management of Cirrhosis of Liver *Proc Staff Meet, Mayo Clin*, 4, 121, April 17, 1929
- ⁹*Idem* End-results of Tying of the Coronary Vein for Prevention of Hemorrhage from Esophageal Veins *Proc Staff Meet, Mayo Clin*, 4, 263, September 4, 1929
- ¹⁰Walters, W Discussion of reference No 3
- ¹¹Walters, W, Rowntree, L G, and McIndoe, A H Ligation of the Coronary Veins for Bleeding Esophageal Varices *Proc Staff Meet, Mayo Clin*, 4, 146, May 8, 1929

SLIDING AND OTHER LARGE BOWEL HERNIAE*
DEVELOPMENT, CLASSIFICATION AND OPERATIVE MANAGEMENT

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THE MOST serious, the rarest, and the most difficult herniae to repair are the sliding herniae of the large bowel. They are the most serious because the bowel forms a part of the sac and mismanagement may not only result in recurrence as in other inguinal herniae but also in the possible development of a fecal fistula and perhaps general peritonitis with disastrous outcome. Since their incidence is estimated at 1 or 2 per cent but few surgeons have an opportunity to operate upon a sufficient number of sliding herniae to really become proficient in handling them. Usually they occur very unexpectedly, and there are no reliable criteria or pathognomonic signs upon which this type of hernia can be diagnosed preoperatively. Unless the surgeon has familiarized himself with the anatomic development of the large bowel and the various relationships assumed in its embryonal circuit, more particularly the second phase of rotation, he may be baffled as to how to proceed. There are perhaps few situations in the abdomen that require more mature judgment and skill than when one is confronted with a large parasaccular or sacless sliding hernia. Walton²⁶ defines a sliding hernia "as one in which some portion of the wall is formed by a viscus which in its normal position is only in part covered by peritoneum." Therefore in its incipency, a sliding hernia is so totally different from the ordinary saccular type, that it is imperative that the surgeon be vigilant at all times, orienting himself in each step to avoid opening the bowel, mistaking it for the wall of the sac, as was done by Sir Frederick Treves²⁴, Lawrence¹⁴, and possibly by others, though unreported, with lethal results. This happened to one patient in our series but the bowel was empty, the opening, which was small, was closed immediately and with the aid of sulfanilamide healed by *per primum*. Also paralleling in importance, after having recognized the type of hernia present, is the possibility of compromising the circulation by boldly dividing the medial or vascular leaflet. In the large or mature sliding herniae there are problems involving the repair of the fascial and other mural structures equal to, if not surpassing any met with in the various saccular types of hernia. We, therefore, feel that sliding herniae, although admittedly rare, are of sufficient importance to justify redescribing their development, classification and operative management. Incidentally we

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are submitting a statistical analysis of 68 cases of large bowel herniae (54 sliding and 14 simple, acquired) in a consecutive series of 2614 repaired inguinal herniae (Table II). This is an incidence of 2 per cent for sliding herniae only.

The literature on saccular herniae, and their repair, is voluminous but, paradoxical as it may seem, it is scanty on herniae of the large bowel including sliding herniae. Moreover this type of hernia was recognized by Galen during the Hellenic Renaissance in Rome, in the second century A. D. Other early writers include Rousselus,²⁸ in 1559, Geiger,²⁸ in 1631, Spigelius,²⁸ in 1645, and Tieves,²⁴ in 1887. In recent years Garnett⁵ (1909), and Bevan⁴ (1930), have made significant contributions which seem to us to portray vividly, and simply, the embryologic evolution, classification, and repair of sliding herniae. In the present communication we have drawn freely from these authors.

TABLE I
TYPES OF SLIDING HERNIAE FOUND

Intrasaccular	27
Parasaccular	26
Sacless	1

TABLE II
OPERATIVE FINDINGS IN 68 HERNIAE OF LARGE INTESTINE

Structures Involved	Sliding Type			Simple, Acquired Type		
	Lt	Rt	Bilat	Lt	Rt	Bilat
Sigmoid	28			8		
Cecum		12			2	
Cecum, ileum and ascending colon		3				
Sigmoid and descending colon	2					
Sigmoid and bladder	1					
Cecum, ileum and appendix		3				
Cecum and appendix		1			1	
Cecum, ileum and omentum					1	
Sigmoid and omentum				1		
Cecum and omentum					1	
Sigmoid and cecum			2			
Total	31	19	2*	9	5	0
Total		54*			14	

* Two patients with bilateral herniae counted as four herniae.

Development and Classification—Carnett classified herniae of the large intestine into the congenital and acquired types. In the congenital type is included those herniae with complete, preformed sacs. The acquired type is subdivided into (a) simple acquired, in which the herniated large bowel is entirely covered by peritoneum and the sac does not form a part of the wall (Fig. 1a), and (b) the sliding hernia in which a portion of the sac is fused with and forms a part of the wall of the herniated large bowel. Sliding hernia may be of the intrasaccular variety (Fig. 1b) with complete sac, or the parasaccular (extrasaccular) variety, with incomplete sac, depending upon the extent of the peritoneal or serous covering of the herniated large bowel (Fig. 1c). A sacless variety occurs but is rare (Fig. 2).

Anomalies in the embryologic development of the small and large bowel are of practical importance to the diagnostician, the roentgenologist and especially the surgeon. Since a sliding hernia is frequently a manifestation of

one of these anomalies, it is essential that the surgeon understand the bizarre conditions that may occur in the rotation of the intestine. It is conceivable to have abnormal disposition of the intestinal loops due to (a) incomplete or nonrotation, and (b) reversed rotation or to deficient fixation. Usually the cecum is completely surrounded by peritoneum except in its attachment to the

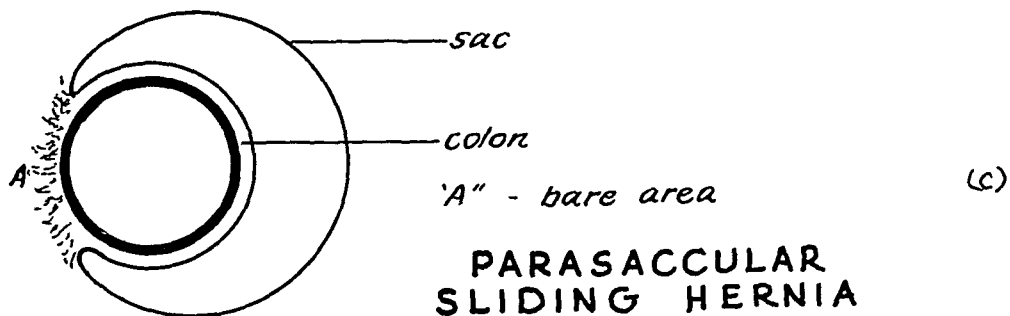
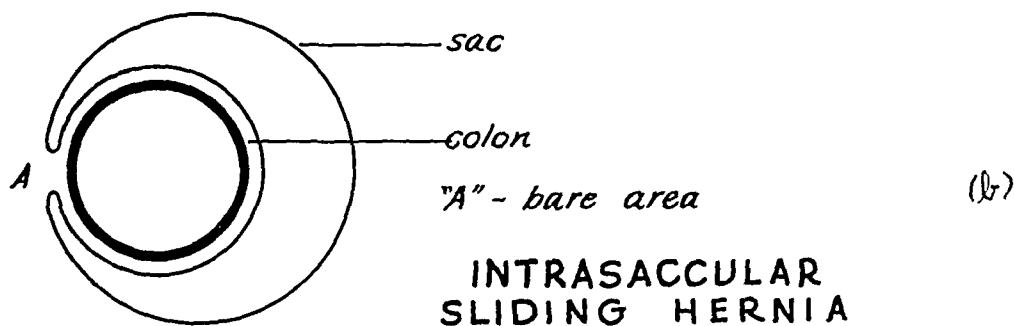
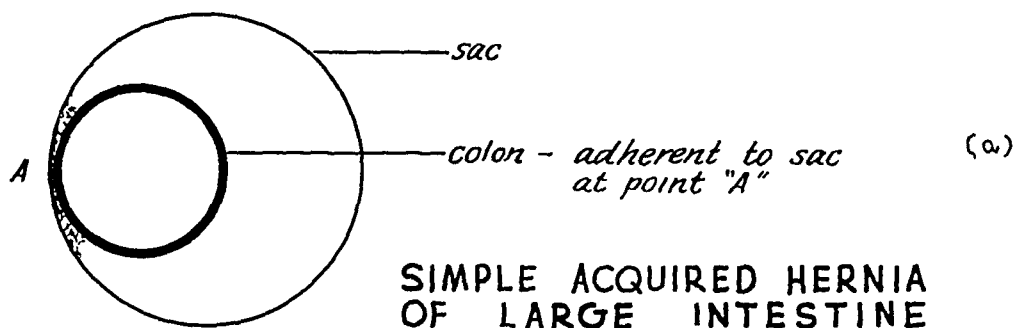


FIG 1—Types of Herniae of Large Intestine

colon and does not possess a mesocolon. However, it may have a mesocecum. Rarely a retroperitoneal cecum may escape by the process of sliding through the internal abdominal ring without its serous covering, thus constituting a sacless sliding hernia.

The sigmoid, which is derived from the hindgut, has been, from the very beginning, an extraperitoneal (termed extraperitoneal by others) structure and has not been involved in the process of rotation. Consequently, in sliding herniae of this structure there is usually a comparatively wide aperitoneal, or bare area, and such herniae are more likely to be of the parasaccular type.

Since the serous (peritoneal) covering of the right and left colon may vary widely, as has already been pointed out in their development, the type of sliding hernia encountered will likewise vary accordingly. Another factor to be reckoned with is the intraluminal and static pressure of the bowel forming the wall of the sac which, if continued for long, may convert an intrasaccular type into a parasaccular one.

The next step in the progress of a sliding hernia is its descent into the inguinal canal. As the peritoneum slides over the underlying connective tissue, the attached oncoming bowel, possibly aided by traction of an unusually long mesentery or by the pull from the hernial sac, appears at the internal abdominal ring. If the ring is dilated, and a preformed sac is present, there should be little resistance to the escape of the hernia into the canal. However, if the sphincter at the internal ring is preserved, it may require wedging and pistoning by the hernial mass before the shutter action is impaired and ring stretched sufficiently to permit

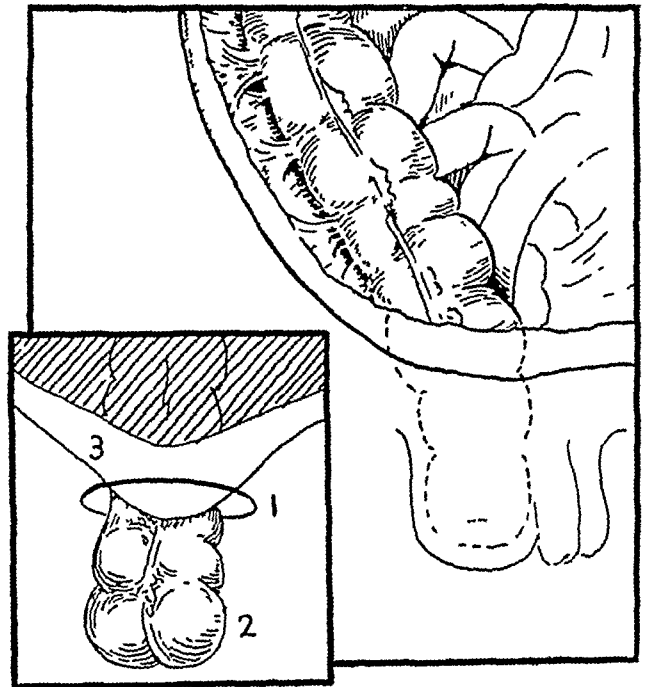


FIG. 2.—Sacless Sliding Hernia of Cecum. 1—Internal ring, 2—Cecum without peritoneum, 3—Peritoneum.

egress of the sliding hernia into the canal, thus manifesting itself clinically as an indirect type. In the event the internal ring holds, then the next most vulnerable area is the inguinal triangle. Here, again, if there is congenital weakness of the muscle component of the internal oblique it would leave the fascia transversalis as the only barrier to the formation of a mature hernia. Usually the fascia transversalis yields to the intermittent intra-abdominal tension and sooner or later becomes weakened. As the pouching increases in size the fascia transversalis becomes more attenuated until there is marked bulging through the floor of the canal. In this instance the sliding hernia would assume the direct type. Where there is generalized mural weakness with loss of obliquity of the canal in the presence of a coexisting congenital sac, the sliding hernia would have the appearance of the combined or indirect-direct type. Therefore, in dealing with inguinal herniae it is easy to see how,

in a few brief moments of dissection, one's attitude can be suddenly changed from one of complacency to consternation

Perhaps the classification of sliding hernia that is most generally used, and a practical one, is that of Bevan⁴. It differs from Carnett's in that it is mainly anatomic rather than embryogenic. Greater stress is placed on the saccular contents than on the extent of the peritoneal investment. Bevan refers to three different forms of sliding hernia: (a) Cecum and ascending colon, (b) descending colon and sigmoid, and (c) the bladder. However, sliding hernia may involve the cecum alone, the cecum and appendix, or the sigmoid alone. At times the mobility of the cecum may be so great as to enable it to assume diverse positions within the abdomen. Therefore, it is possible to have the cecum in umbilical, left inguinal, and femoral herniae (Hildebrand¹¹, and Gibbons⁸). Fortunately, these abnormalities in disposition are rare. The attachment of the peritoneal sac to the bladder for a distance of one to two inches is by no means unusual, occurring in 63 per cent of inguinal herniae in our series. Before diagnosing a sliding hernia of the bladder, one should make sure that the bladder wall actually prolapses into the canal and constitutes the primary bulging and not simply auxiliary to the hernial mass. Of course, a concomitant bladder attachment is more frequent in direct or bilocular herniae.

Diagnosis—A diagnosis of sliding hernia preoperatively cannot be unequivocally established. However, there are certain criteria which cause one to suspect such a hernia. Frequently the patient will relate that he has had a hernia for some time, perhaps several years, and that it has been getting progressively larger. In our series there were a few exceptions to this rule in which the herniae were of a few months duration and had attained considerable size during that brief period. The patient may state that he is unable to wear a truss because of the increased pain during its use. On examination, a dilated external, as well as internal, ring is usually found. Owing to the compromise of function of muscular and fascial structures, there is loss of obliquity of the inguinal canal. A large hernial mass frequently extends down into the scrotum and contains bowel. An attempt to completely reduce this mass may be unsuccessful and give rise to pain. A barium enema may reveal a loop of large bowel in the hernial sac. In the congenital type, traction on the testis after the hernia is reduced causes the hernia to reappear.

Repair of the Sac—The first prerequisite in the repair of herniae of the large bowel, the vast majority of which are sliding, is the total obliteration of the sac, with the best possible closure of the stump. When dealing with a simple, acquired hernia of the large intestine the adhesions between the bowel and sac are divided and the intestine returned to the abdominal cavity. The sac may then be freed and closed usually by torsioning an suprasacculal ligation, as described by Russell²³, which is routinely done in all of our inguinal hernia repairs.

On the other hand, when dealing with a sliding hernia, the closure of the sac is a more difficult undertaking. The bowel forming a part of the sac wall

must first be mobilized in order to permit its reduction and proper closure of the sac. To accomplish this safely one must have a thorough knowledge of the blood supply to the involved intestine (Fig 3). The freeing of the bowel without consideration of this factor may lead to circulatory impairment and gangrene of the involved segment. In the formation of a sliding hernia, we must remember that as the bowel moves or glides down through the internal ring the nutrient vessels are carried along with it. From a study of the anatomy of the large bowel we learn that the blood supply to the colon (except the rectum) enters by way of the medial leaflet of the mesocolon, a fact long recognized, and made use of practically, in successful colon surgery. The lateral leaflet of the mesocolon is avascular. Consequently, in freeing a loop

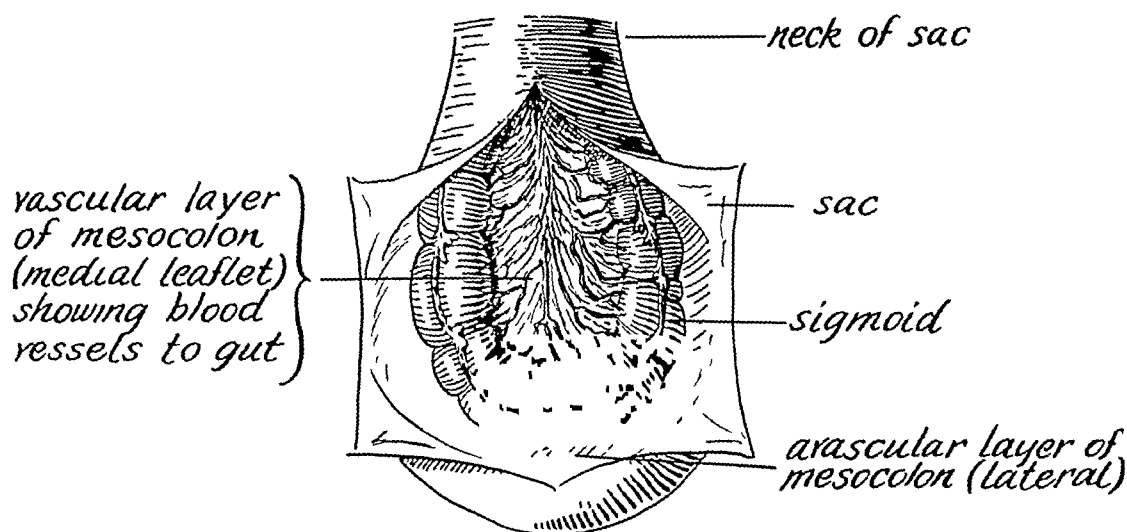


FIG 3 —Blood supply to intestine in sliding hernia

of large bowel in a sliding hernia, the lateral leaflet of the mesocolon may be cut with impunity but the medial leaflet must not be disturbed.

In our routine repair of direct, bilocular and other inguinal herniae, we follow Hoguet's¹² technic of freeing the sac and all variants of the sac are indirectized. The sac is dissected from the bladder whenever such dissection is necessary for adequate high ligation. Our statistics reveal that such a dissection of bladder from the sac was necessary in 63 per cent of inguinal herniae repaired exclusive of sliding herniae. In sliding herniae such a dissection was necessary in but 20 per cent of those repaired.

Several methods of handling the sac in the repair of sliding herniae can be found in the literature. That of Bevan (Fig 4) may be considered as being perhaps the most satisfactory, especially for the parasaccular type. He incises the avascular or lateral fold of peritoneum of the mesocolon, thereby freeing the bowel. He then raises the bowel and unites the peritoneal flaps behind it but perpendicular to the incision which in effect lengthens the mesocolon permitting reduction of the large intestine forming the wall and at the same time covering the raw surface. This is the same principle which has been employed by Heineke¹⁰, Mikulicz¹⁹, and W J Mayo¹⁷, in correcting stenoses of hollow viscera, particularly at the pylorus. After having replaced

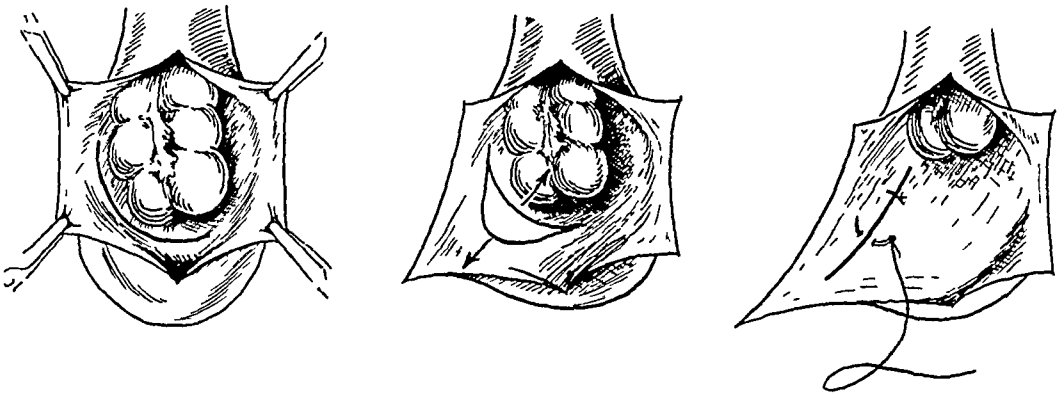


FIG 4—Bevan's method of sac closure in sliding hernia

the bowel in the abdomen the sac is invaginated by means of a series of purse-string sutures, which forms a tampon or cushion at the internal ring

Carnett describes a method employed by Morris²¹, van Heuverswyn²⁵, Gouillard,⁹ and others (Fig 5) The sac is incised on either side of the reflection of the peritoneum a short distance from its junction with the intestine, thereby producing a free flap of peritoneum on either side of the bowel. Each flap is then turned back behind the bowel so as to cover the bare area and the two are sutured together in this position forming a sort of mesocolon

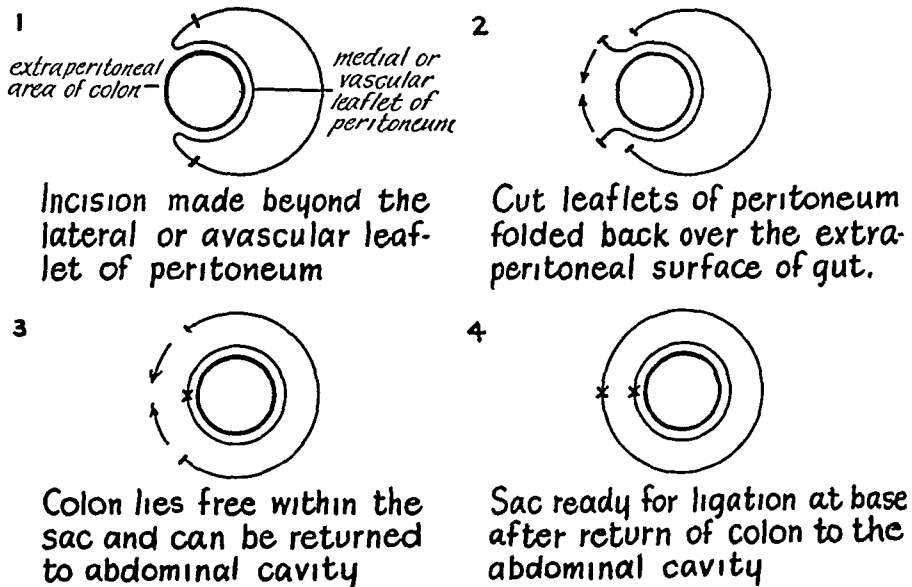


FIG 5—One method of handling sac in sliding hernia (view looking down into the sac)

In the suturing of these flaps care should be exercised to avoid traumatizing the vessels in the medial leaflet. The cut margins of the sac are then brought together and sutured, so that the intestine now lies completely within the sac. The bowel is then pushed into the abdominal cavity and the neck of the sac is closed. If used with caution this method is of value especially in cecal herniae.

Another method of obliterating the sac is that of Berger³ which differs from Carnett's in that the uncut peritoneum on either side is united behind

the bowel, thus forming a mesocolon covering the denuded area. The stump of the sac is then transfixed beneath the internal oblique and transversalis muscles, as originally described by Ball² (1884), and subsequently by Kocher¹³ (1892).

In some instances in our series of sliding herniae, we have deviated somewhat from the previous methods in that a fish-mouth-type of closure of the sac has been used (Fig 6). This method consists in overlapping that half of the sac which does not contain bowel over the other half which contains the freed and reduced sliding loop of intestine. Therefore, in this arrangement, the anterior surface of the bowel is covered by a double layer of peritoneum.

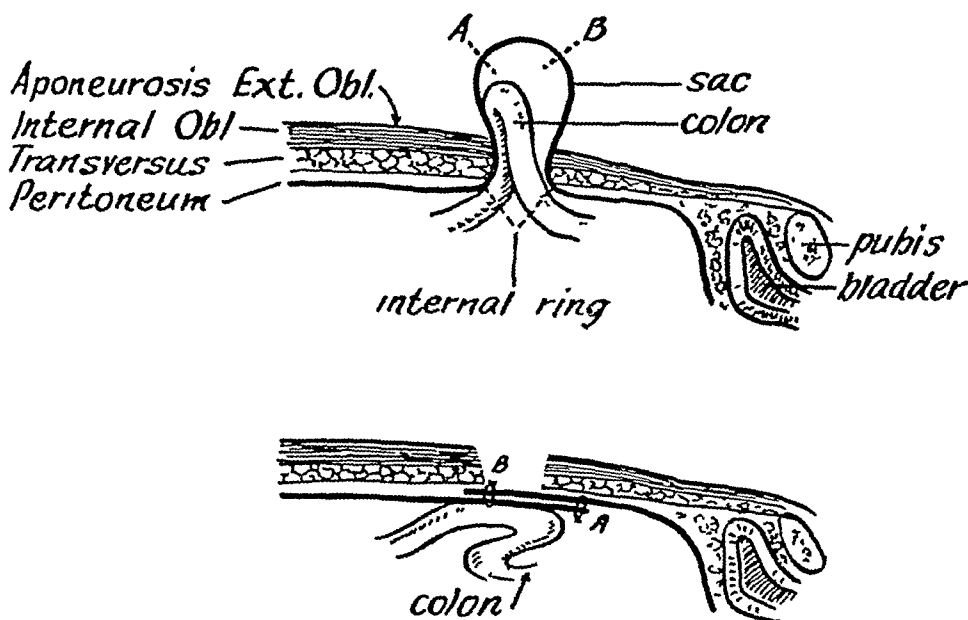


FIG 6—Fish mouth closure of sac in sliding hernia

Repair of the Wall—Since herniae of the large intestine are usually of good size, often with concomitant marked structural weaknesses at the internal ring and the floor of the canal, we consider the repair of the wall in such herniae of utmost importance. In the majority of these herniae, particularly the intrasaccular and simple acquired types occurring for the first time, we have employed the method of Ramos and Burton²². This method differs from the original Andrews¹ procedure in the placing of the cord extra-aponeurotically instead of interaponeurotically, and the careful denudation of the transversalis fascia of any muscle fibers. It is an all-fascia closure, obtained by suturing the fascia transversalis to the recurved edge of the inguinal ligament, with imbrication of the aponeurotic flaps of the external oblique muscle. This method is based upon principles which are physiologically and histologically sound. It may be used with considerable satisfaction in those instances where there is no attenuation or absence of the fascia transversalis and no structural weakness of the inguinal ligament. In our series, 50 primary herniae of the large bowel were repaired by this

method Twenty-five of these were followed for an average of 34 months, with three recurrences (Table III)

TABLE III
FOLLOW UP STUDY AT YEARLY INTERVALS OF 43 SLIDING HERNIAE

Follow-Up—in Months	Number of Cases	Recurrences
72 to 84	5	0
60 to 72	2	0
48 to 60	4	0
36 to 48	5	1
24 to 36	5	0
12 to 24	22	2
Average months 34	Total 43	3 or 6.9%
Exam by physicians	27	2
Direct correspondence	16	1

TABLE IV
TYPES OF REPAIR—NUMBER FOLLOWED AND RECURRENCES OF HERNIAE OF LARGE INTESTINE

	Number of Operations	No. Followed	Recurrences
Triplicate fascial closure	50	25	3
Fascial sutures (Gallie ⁷ and McArthur ¹⁸)	14	14	0
Cooper's ligament	2	2	0
Pedicled fascial graft	2	2	0

In primary herniae of the large intestine, with attenuation of the fascia transversalis, we employ a fascial suture according to the method of Gallie,⁷ or McArthur¹⁸ Fourteen herniae have been repaired by this method, with no recurrences

In recurrent sliding herniae the mural repair is a more formidable undertaking Usually careful evaluation of the structures will reveal marked thinning or absence of the fascia transversalis, which requires replacement by like tissue without tension if reasonable success is to be expected In the two cases encountered in our series we elevated a pedicled-graft of fascia lata, passing it through the femoral canal and then fanning it out and uniting it to the lateral edge of the rectus sheath This is a modification of Wangenstein's²⁷ method Those herniae recurring a second or third time should also be repaired by this method The two cases in which this method was used have been followed two years, without recurrence

Where there is fragmentation or inadequacy of Poupart's ligament but with strong and retentive fascia transversalis, termed endo-abdominal fascia by Dickson,⁶ Cooper's ligament should be used for anchorage in lieu of Poupart's, as originally described by Lotheissen¹⁵ (1898) Follow-up examinations in the two cases in which this type of repair has been used reveal the most resistant walls of any repairs we have used In fact, we have been so favorably impressed that we are employing this technic in an increasing number of cases, especially in those having marked laxity of the floor

HERNIOCELIOTOMY

Some of the more adventurous surgeons have introduced a celiotomy in addition to the usual methods of obliterating the sac and repair of the wall Their contention is that the better exposure permits of greater dissection of the dislocated loop, enabling reduction of the bowel to its former position

and then fixing it in this position by some type of colopexy. A second consideration pointed out by those favoring this method is that the bowel is suspended and does not rest on the internal abdominal ring as in the usual hernial repair. Theoretically the hernioceliotomy may possess certain advantages over the routine plastic procedures that are generally employed, but the complications which may obtain by introducing another incision and the consequent trauma outweigh the theoretic advantages. We, therefore, believe as does Bevan, who states "It is very desirable not to complicate the operation with a laparotomy." Moreover, with a recurrence rate of only 6.9% in our series, we are reluctant to change our basic ideas in dealing with sliding herniae until greater success has been shown by other methods than is apparent in the statistics so far reported. In those massive herniae in which the fascial floor no longer offers any resistance to the egress of the bulging mass, and perhaps the type ideally suited for a celiotomy, we feel that the retentive structure can be replaced successfully by using a pedicled-graft of the iliotibial tract of fascia lata.

In deference to those surgeons who are exponents of hernioceliotomy, reference is made to Morestin's²⁰ method. After disposing of the sac, as does Berger,³ he makes another incision through the abdomen, withdraws the bowel and sutures the base of the newly formed mesocolon to the iliac fascia. The inguinal repair is completed in the usual manner. MacKidd¹⁶ uses the bi-incisional technic, replacing the sliding loop of bowel and fixing it there. He then corrects the redundant peritoneum by overlapping the lower loop on the upper, which produces a double layer of peritoneum over the front of the bowel. In the repair of the canal, the aponeurotic flaps are imbricated without transposition of the cord and without using the fascia transversalis or internal oblique muscle, or disturbing the relationship of the funicular structures.

SUMMARY

1 The embryologic development, classification and diagnosis of inguinal herniae of the large intestine have been discussed.

2 The operative findings in 68 herniae of the large bowel have been tabulated.

3 Methods of closure of the sac and the complications that arise in mobilizing the bowel have been redescribed.

4 Indications for various technical procedures in the repair of the wall in primary and recurrent sliding herniae have been discussed and evaluated. The types of operations performed in this series have been tabulated.

5 A statistical analysis of 2,614 consecutive inguinal herniae repaired at this hospital reveals that 68 were herniae of the large intestine. Of these, 54 were the sliding type, and 14 the simple, acquired type. The sliding herniae formed two per cent of all those repaired. Forty-three primary sliding herniae, followed for an average of 34 months, showed a recurrence rate of 6.9 per cent.

REFERENCES

- ¹ Andrews, Edward Wyllys Imbrication or Lap-Joint Method A Plastic Operation for Hernia The Chicago Medical Recorder, August, 1895
- ² Ball, C B The Radical Cure of Hernia by Torsion of the Sac Brit Med Jour 1, 461, 1884
- ³ Berger Bull Med, Paris, 20, 613, 1906
- ⁴ Bevan, Arthur Dean Sliding Hernias of Ascending Colon and Cecum, the Descending Colon and Sigmoid, and of the Bladder ANNALS OF SURGERY, 92, 754, October, 1930
- ⁵ Carnett, John Berton Inguinal Hernia of the Cecum, ANNALS OF SURGERY, 49, 491, April, 1909
- ⁶ Dickson, A R Femoral Hernia Surg, Gynec and Obst, 63, 665, 1936
- ⁷ Gallie, W E, and LeMesurier, A B Living Sutures in the Treatment of Hernia, Canadian Med Jour 13, No 7, 1923
- ⁸ Gibbon J A M A, 30, 1385, 1898
- ⁹ Goullard et Rafin These de Lyon, 1897
- ¹⁰ Heineke Reported by F Fronmuller, Operation der Pylortenoze, Inaug—Dissert, (Erlangen), Furth, 1886, P 13
- ¹¹ Hildebrand Deut Zeit f Chir, 33, 82, 1892
- ¹² Hoguet, J P Direct Inguinal Hernia ANNAIS OF SURGERY, 72, 671-674, December, 1920
- ¹³ Kocher, T Zur Radical Cur der Hernien Cor Bl f Schweiz, Aerzte, 22, 561-576, 1892 Also Transl ANNALS OF SURGERY, 26, 505-526, 1892
- ¹⁴ Lawrence Treatise on Rupture, 5th Edition, London, 1838
- ¹⁵ Lotheissen, G Radical Operation for Femoral Hernia Zentralbl f Chir, 25, 548, 1898
- ¹⁶ MacKId, L S Inguinal Hernia With Special Reference to Sliding Hernia—A New Treatment The Canadian Med Assoc Jour, 34, 269, March, 1936
- ¹⁷ Mayo, C H Gastroduodenostomy Surg, Gynec & Obst, 38, 583, 1924
- ¹⁸ McArthur, L L Autoplastic Suture in Hernia and Other Diastases Preliminary Report, J A M A, 37, 1162, 1901 Final Report, J A M A, 43, 1039, 1904
- ¹⁹ Mikulicz, J Zur Operativen Behandlung des Stenosirenden Magengesch Wures Arch f klin, Chir, 37, 79, 1888
- ²⁰ Morestin Congr franc de chir, 1900
- ²¹ Morris Lancet, 2, 979, October 19, 1895
- ²² Ramos, Raoul L, and Burton, Claude C Inguinal Hernia Application of Cardinal Principles in the Repair of Inguinal Hernias Surg, Gynec & Obst, 69, 688-693, 1939
- ²³ Russel, R Hamilton Inguinal Herniae Their Varieties, Mode of Origin and Classification Brit Jour Surg, 9, 502, 1922
- ²⁴ Treves, Frederick, Sir Hernia of Cecum Brit Med Jour, 1, 382, 1887
- ²⁵ van Hueverswyn Jour des Sci Med, de Lille, 16, 121, February 10, 1893
- ²⁶ Walton, Albert J Extrasaccular Hernia ANNALS OF SURGERY, 47, 86-105, 1913
- ²⁷ Wangenstein, O H Repair of Recurrent and Difficult Hernias and Other Large Defects of the Abdominal Wall Employing Iliotibial Tract of Fascia Lata as a Pedicle Flap Surg, Gynec & Obst, 59, 766, 1934
- ²⁸ Watson, L F Hernia, 2nd Edition, St Louis, C V Mosby Co, 1938

SPIGELIAN HERNIA

SPONTANEOUS LATERAL VENTRAL HERNIA THROUGH THE SEMILUNAR LINE

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THE LINEA SEMILUNARIS (Spigelii) is the line of transition between the muscle bundles and aponeurosis of the transversus abdominis muscle. Its convexity is outward, it lies farthest from the rectus margin at the level of the umbilicus, decreasingly distant from there downwards. It does not coincide with the line of transition in the internal oblique, which, unless extreme muscular aplasia exists, follows the rectus margin quite closely. Lateral to the rectus and medial to the muscular portion of the transversus, the aponeurosis of the latter is almost inseparably adherent to the posterior surface of the internal oblique muscle. However, and particularly at the point where the aponeurosis passes forward and fuses with that of the internal oblique, there are found numerous, up to 3-4 mm, irregular slit-like defects. It is here, at the junction of the semilunar and semicircular (Douglas') lines that almost all reported lateral ventral herniae have been found, i e, lateral to the rectus, medial to the muscular portion of the transversus, and at or below the fold of Douglas, which usually forms part of the ring. It is possible that these defects are widened by the outward pull of the accessory slip of internal oblique described by Chouke¹⁰ as occurring in a majority of individuals. They certainly vary with the major variations in Douglas's fold, described by him, and by McVay and Anson^{10a}.

Many authors, following the anatomic studies of Ferriand,^{1a} Thevenot and Gabouird,²⁵ and Beaudoin,⁶ have ascribed great etiologic significance to a lateral branch of the deep inferior epigastric artery traversing one of these defects. Koljubakin,¹⁸ alone amongst others who have searched for them, has found them with frequency, anatomically, or reported them as emerging through the hernial ring^{12, 17, 19, 23}. There is a relatively constant small lateral branch of this artery running upwards and outwards behind the rectus. It is not constant in the point of passage into or through the transversus, it lies in front of the transversalis fascia hence not piercing that important structure. The defects commonly seen are larger than any through which I have seen this artery pass. The artery probably has slight etiologic importance. Peritoneal lipoma preceding the hernia has been frequently described. It may be noted here that the relatively uncommon direct inguinal hernia with a small tight neck, a prehernial lipoma and a marked tendency to strangulation is a hernia through Spigel's line, emerging through, rather than below, the transversus aponeurosis. The frequency with which semilunar line hernia has occurred in the subjects of other herniae, and

with straining, in subjects with weakened abdominal walls impels one to consider congenital susceptibility, muscular atrophy, pregnancy, obesity, emaciation, chronic cough and severe muscular effort as immediate predisposing factors

Although spontaneous lateral ventral hernia had long been known, Klinkosch was the first, in 1864, to locate it specifically in Spigel's line. Since that time, there have been many anatomicosurgical reviews of collected cases^{1, 2, 4, 5, 10, 18, 19, 20, 26}. Allowing for duplications, and excluding cases unquestionably not spigelian hernia, there have been 99 true spontaneous cases reviewed, I have been able to find reports of 13 additional,^{8, 9, 12, 15, 17, 22, 23, 24, 25} making, with the four here to be reported, 116. Only four cases are reported in the American literature^{11, 15, 16, 28}. There is one collective review,¹⁶ and one good textbook account.²⁷ In the 20 years since Holloway,¹⁶ and Auge and Simon⁴ reviewed a total of 58 cases, one case has been reported in America, 53 elsewhere.

The hernial ring is lateral to the rectus margin, seldom above Douglas' fold, lying at the juncture of the middle and outer thirds of a line from anterior superior spine to umbilicus. It may be from 0.5 cm to 2 cm in diameter, seldom larger. Bonetto⁸ described one of 4 cm. The edges are a sharply defined defect in the transversus aponeurosis. The upper, and upper-lateral margins are made crescentic and sharper by the edge of Douglas' fold.

The sac is formed of peritoneum and occasionally fibers of the transversalis fascia. Its thickness seems to depend on duration. It penetrates the transversus aponeurosis and the internal oblique muscle or aponeurosis. It may then spread beneath the external oblique aponeurosis, seldom perforating this relatively free layer. Hence, the hernia is commonly intraparietal, the "masked" hernia of Macready. The sac may be from pea to orange size. Enormous herniae have been described by Jaboulay,⁴ Le Marie and Pitschke,⁴ Lobello,¹⁹ and Fournier.¹⁴ Brandtner,⁹ Berger,⁷ and Nystrom²¹ reported bilateral spontaneous semilunar herniae. Coley¹¹ felt that the semilunar hernia he reported was traumatic in origin, but the typical location and character of the ring, the interparietal sac, and the presence of indirect and direct inguinal herniae suggest that the indicated fall was only incidental. Steimker⁴ observed a similar case at autopsy. Golderger and Panebianco¹⁵ described a large hernia in the semilunar line above the umbilicus, associated with epigastric, para-epigastric and umbilical herniae. Scopinaro²⁴ examined in life and at necropsy a six-day-old infant with congenital strangulated spigelian hernia in which a fecal fistula formed. Two brothers had died at seven days and six weeks of age respectively, of identical conditions. The father had bilateral inguinal herniae.

Adhesions, with irreducibility, incarceration and strangulation have been commonest in the larger herniae. Small intestines and omentum are the common contents of the sac, colon rarely. In Case 1 of this report a sliding spigelian hernia of the sigmoid was found. Beaudoin described a multi-

locular, and apparently sliding, spigelian hernia containing cecum, appendix, small intestine, and omentum. The sac in Teales' case contained colon.¹⁶ I was able to find only these two cases resembling Cases 1 and 2 of this report.

Spigelian herniae, even of fair size, may be symptomless. They may cause mild to severe localized or more diffuse neuralgic pain, aggravated by straining and relieved by spontaneous or manual reduction of the hernia.

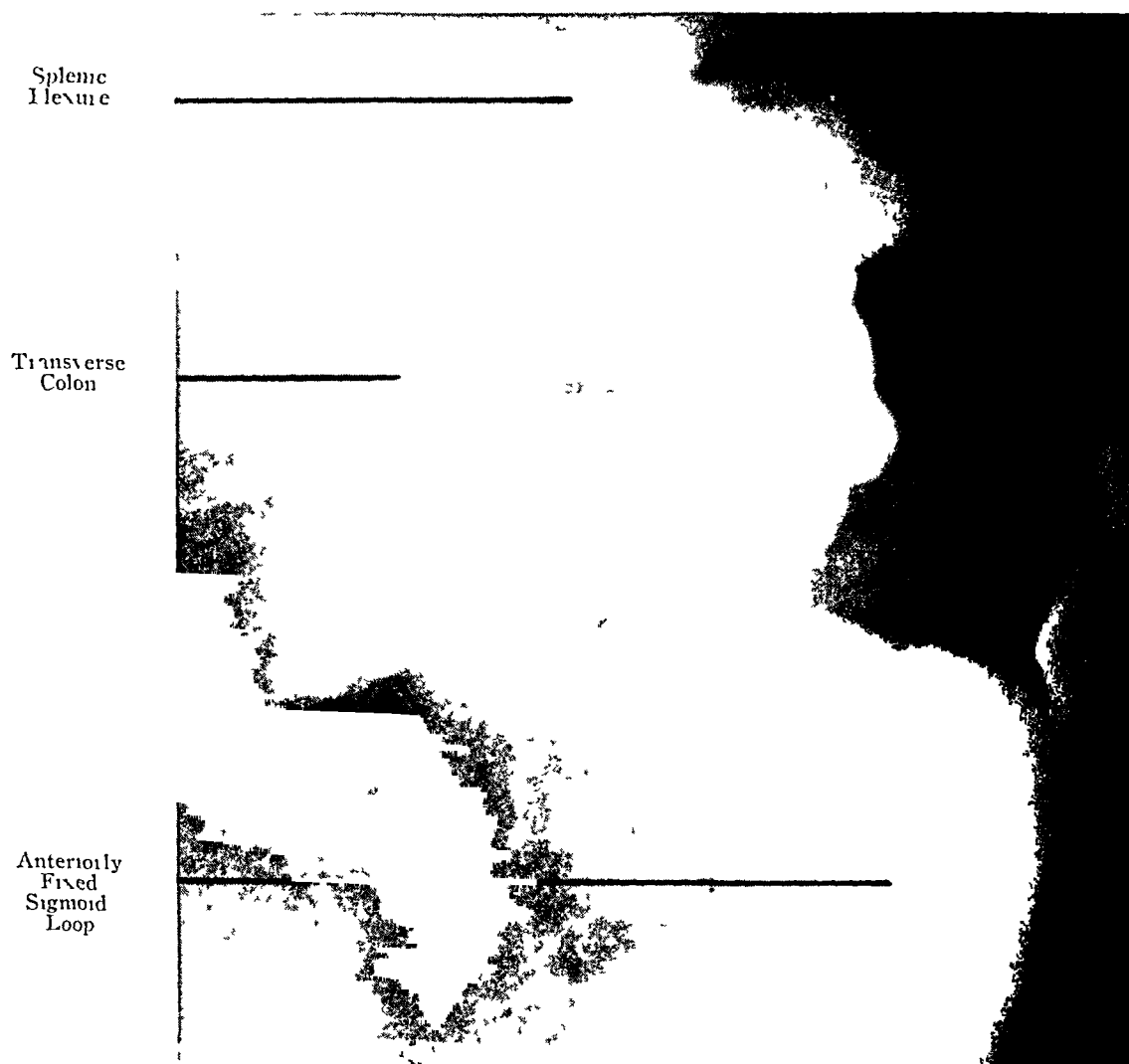


FIG 1—Case 1. Lateral roentgenogram showing the anterior fixation of the sigmoid loop, postoperatively.

It may be impossible to palpate a small interparietal mass, especially in an obese patient. However, a localized point of tenderness in the abdominal wall, significantly located at the site of the ring, can usually be found. Watson²⁷ feels this to be best elicited in the erect position. It has seemed to me best demonstrated by palpating along the rectus margin of the supine patient, straining to raise the head and shoulders. This procedure quite definitely excludes visceral tenderness.

The four herniae, upon which this report is based, were spontaneous, interparietal and located at the junction of semilunar and semicircular lines. One was large, multilocular, incarcerated, and strangulated. One was a sliding hernia.

Case 1—A W, age 64, a well-developed, well-nourished male, had done strenuous work in his youth, extensive walking during the past 10 years had been with effort because of an arthritic hip. Two years ago (one year after an operation for strangulated right indirect inguinal hernia), he noted a "lump" on the left side, easily reducible by pressure with his left thigh flexed. When it protruded, especially in the morning, he had

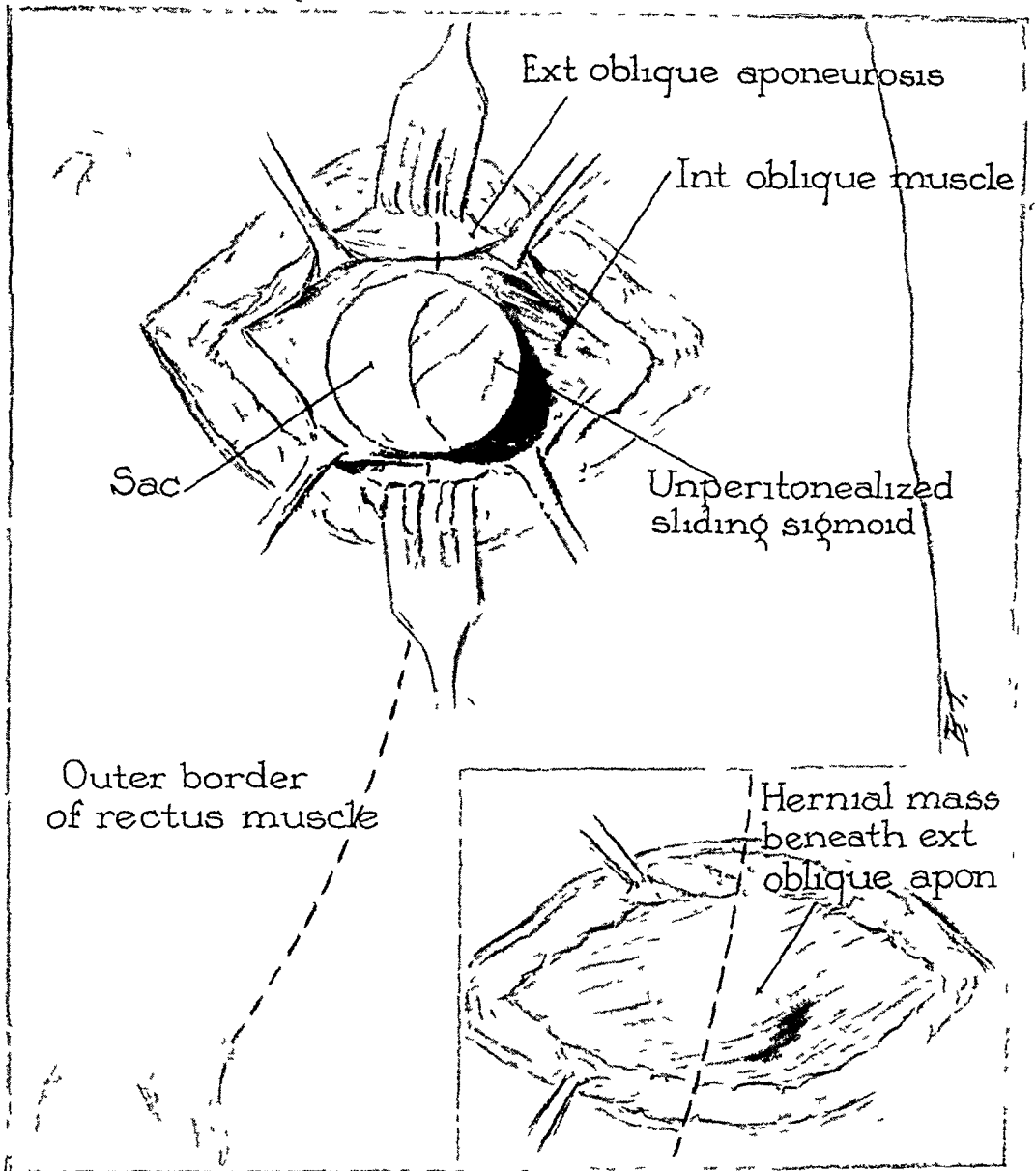


FIG 2—Case 1 Showing anatomic relations of the structures involved, as noted at operation

a dull aching pain and distress from "gas." He blamed his constipation on the lump, stating that if he held it reduced he could pass gas and have his usual morning bowel movement. On three occasions I was unable to palpate the mass or the ring, and he could not produce the lump by straining. On November 1, 1937, he came in saying the lump was then present. An indefinite mass was palpable at the lateral margin of the rectus muscle at the level of the anterior superior spine. It disappeared with a gurgle upon lying down, the area remained moderately tender to deep palpation. No ring was felt. He was admitted to Oak Park Hospital.

Operation—November 2, 1937 Under novocain block, a transverse incision was made at the level of the anterior superior spine. The ring was about 2 cm in diameter, and the thickened margin consisted of transversus and internal oblique fibers. When he strained the sac protruded to a height of about 3 cm beneath the external oblique aponeurosis. The lateral wall of the sac was unperitonized sigmoid colon.

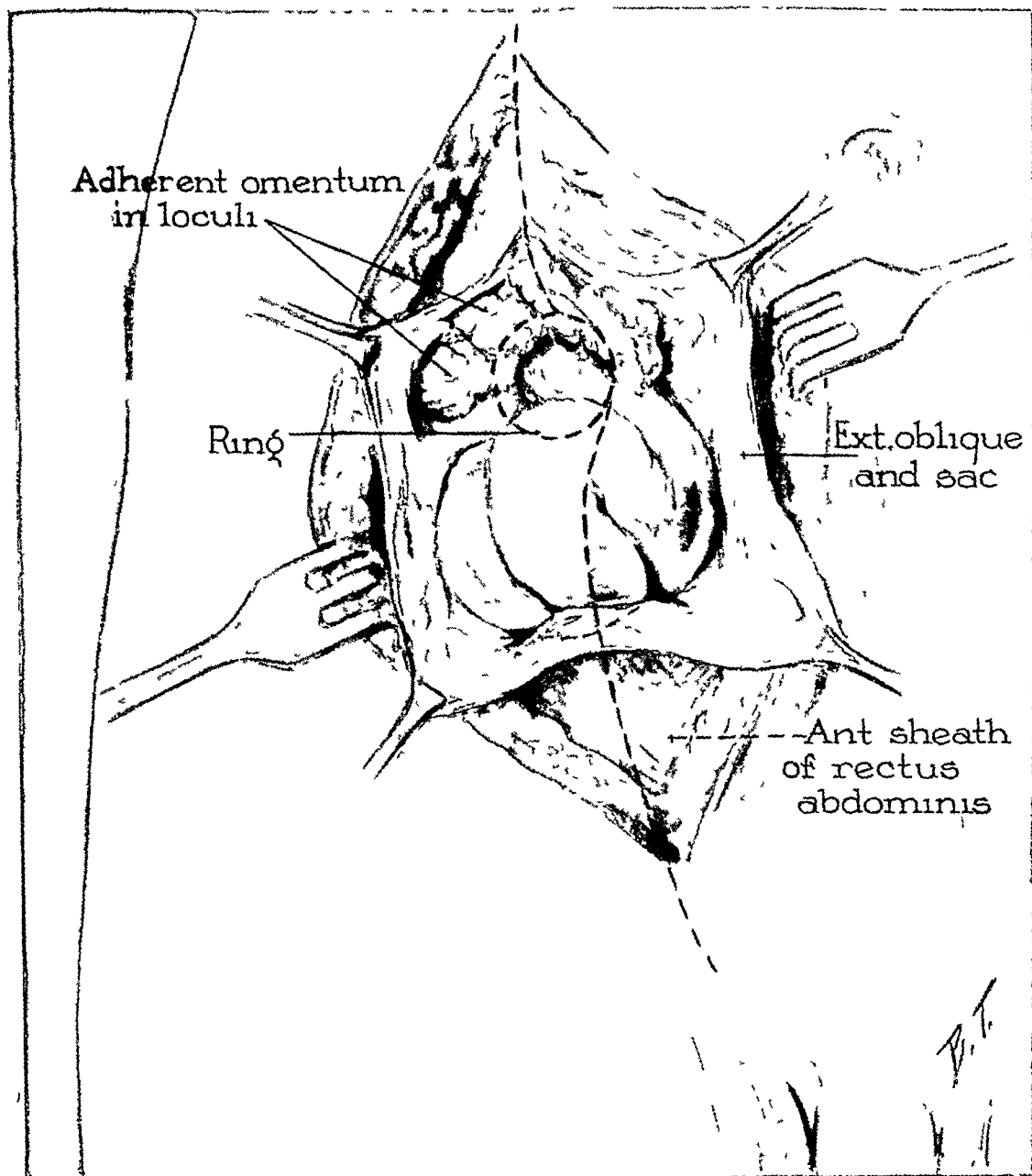


FIG 3—Case 2 Showing anatomic relations of the structures involved, as noted at operation

The incision in the sac was closed, the intestine pushed back, and the peritoneal suture anchored to the lateral angle of the transversus aponeurosis. Closure was by transverse imbrication of the ring margins and simple closure of the external oblique. Recovery uneventful, and he has remained well since.

Case 2—T. M., a well-developed, well-nourished, somewhat obese male, age 54, was admitted to the Cook County Hospital, August 6, 1939, at 7:30 P. M. He complained of colicky abdominal pain, nausea and vomiting, and obstipation for 48 hours. He had had a hernial mass in the right lower quadrant lateral to an old midrectus scar, slowly increasing in size for 20 years. The abdominal pain seemed to have

originated at that point Twenty-four hours previously a physician had unsuccessfully attempted reduction The past history was irrelevant except for appendectomy in 1914 He had never paid much attention to the hernia

His abdomen was obese, there was doughy distention, the bowel sounds were infrequent and obstructive in character There was a large, bulging, irregular, firm, poorly defined mass in the right lower quadrant, lateral to the old scar The contents of the lower half of this irregular loculated hernia were reducible, of the upper, more tender portion, irreducible His general condition was good

Operation—Under spinal analgesia, an oblique incision over the mass was made through skin and external oblique aponeurosis Lying between the external and internal obliques, the hernial sac had four walnut-sized loculations surrounding a 2.5 cm circular defect in the transversus and internal obliques at the junction of semilunar and semicircular lines The right rectus muscle was thin and atrophic Extending down to the inguinal region was a loculation of orange-size This contained reducible loops of undamaged ileum, the four small ones contained adherent incarcerated omentum which was especially adherent to the ring No defects were palpable at the umbilicus, the right inguinal and femoral rings or the inner surface of the appendectomy scar After dissection and resection of the involved omentum, clean definition of the defect, and closure of the peritoneum, the transversus aponeurosis was imbricated transversely with interrupted mattress sutures of silk The lining of the lower part of the sac was imbricated over this and the external oblique and skin closed He made an uneventful recovery, and upon examination, February 10, 1941, had no palpable recurrence

Case 3—V A, age 21, single, a well-developed, thin, white female, had had attacks of right-sided pain and soreness for a year It had been said to be due to appendicitis The pain disappeared on lying down and had no relation to alimentary rhythm There was a small tender area, to which she pointed accurately, in the semilunar line just above the level of the anterior superior spine No mass or ring was felt

Operation—January 29, 1939, at Oak Park Hospital A transverse incision was made The internal oblique muscle was intact but thin, almost aponeurotic There was a 1.5 cm elliptical defect in the transversus aponeurosis, the upper margin being the fold of Douglas, through which the peritoneum bulged Closure as in Case 1 The appendix was grossly and microscopically normal Recovery was uneventful, and relief has been complete

Case 4—A S, age 35, married, multiparous, a well-developed, well-nourished white female, had had almost similar pain, also disappearing upon reclining She had had a supracervical hysterectomy in 1936, and had been told that her residual left-sided pain was due to a slightly cystic left ovary No mass or ring was felt at the tender spot

Operation—August 3, 1939, at West Suburban Hospital A one centimeter elliptical defect in the transversus and internal oblique was found, slightly above the level of the anterior spine She has remained free of pain following repair

SUMMARY

1 The anatomy of the transversus aponeurosis is reviewed, and observations pertinent to the etiology of semilunar line hernia added

2 Case reports appearing since the last collective review are noted

3 Constant location, interparietal "masked" character, and apparently frequent strangulation are noted as leading to the belief that the hernia when small and uncomplicated is possibly frequently overlooked as a cause of pain

4 Four cases are reported

BIBLIOGRAPHY

- ¹ Angeletti, E Spigelian Hernia Review Arch Ital di Chir , 17, 38-60, 1927
- ² Anzilotti, E , Clinical and Therapeutic Study of Three Cases of Spigelian Hernia Arch Ital di Chir , 50, 107-119, 1938
- ³ Apfelthaler, M On the Occurrence of Ventral Spigelian Hernia Zentralbl f Chir , 51, 1680, August 2, 1924
- ⁴ Auge, A, and Simon, R Contribution to the Study of Hernias in the Semilunar Line of Spigel Rev de Chir , 59, 297, 1921
- ⁵ Barthelemy, M Lateral Abdominal Hernias Bull et Mem Soc de Chir , de Paris, 45, 1313-1319, October 15, 1919
- ⁶ Beaudoin, Quoted by Holloway ¹⁰
- ⁷ Berger Quoted by Barthelemy, ⁵ and Holloway ¹⁰
- ⁸ Bonetto, E, Ventrolateral Hernia of Linea Semilunaris Rif Medica, 54, 875-877, June, 1938
- ⁹ Brandtner, C E Case of Traumatic Hernia in the Spigelian Line Arch fur orthopadische und Unfall-Chirurgie, 33, 219, 1933
- ¹⁰ Chowke, K S The Constitution of the Sheath of the Rectus Muscle Anat Record, 61, 341-348, June, 1938
- ^{10a} McVay, C B, and Anson, B J Composition of the Rectus Sheath Anat Record, 77, 213-225, June, 1940
- ¹¹ Coley, W B Interparietal Ventral Hernia at McBurney's Point ANNALS OF SURGERY, 50, 246-249, 1909
- ¹² Derycke, P Contribution to the Study of So-called Hernia of the Zone of Spiegel Bruxelles Med , 18, 85, May 1, 1938
- ¹³ Ferrand J A M J, Quoted by Thevenot and Gabourd ²⁶
- ¹⁴ Fournier, R Hernia of Spigel's Line Bull Soc d'obst et Gynec , 22, 695, October, 1933
- ¹⁵ Goldberger, H A, and Panbianco, R R Multiple Hernia Am Jour Surg , 42, 423, November, 1938
- ¹⁶ Holloway, F Spontaneous Lateral Hernias ANNALS OF SURGERY, 75, 677, June, 1922
- ¹⁷ Junet, W Hernia of the Semilunar Line of Spiegel Acta Helvet Med , 4, 403, August, 1937
- ¹⁸ Koljubakin, S L Hernia of Spigels' Line Arch f klin Chir , 136, 739, 1925
- ¹⁹ Lobello, F Contribution to the Knowledge of Spontaneous Hernia of Spigels' Line Riforma Med , 50, 525, April, 1934
- ²⁰ Mackrocki Quoted by Auge and Simon ⁴
- ²¹ Nystrom, G Two Cases of Hernia of Linea Spigelii Acta chir Scandiu , 56, 92-95, 1923
- ²² Odes, L A Hernia of the True Semicircular Line of Spigel Vestnik Khir , 44, 49, 1936
- ²³ Papin, F Strangulated Hernia of Linea Semilunaris Spigelii Bordeaux Chir , 7, 203, April, 1936
- ²⁴ Scopinaro, A J Hernia on Spigels' Semilunar Line in a Newborn Semana Medico, 1, 284, January 24, 1935
- ²⁵ Seara, P Anatomico Surg Study of the Line of Spigelius Pathology of Spigelian Hernia Dia Med , 10, 972, September 19, 1938
- ²⁶ Thevenot, L, and Gabourd, T Spontaneous Hernias of the Semilunar Line of Spigel Rev de Chir , Paris, 35, 568-585, 1907
- ²⁷ Watson L F Hernia, 2nd ed p 370, St Louis C V Mosby, 1938
- ²⁸ Watson Hernias of Upper Abdomen Memphis Med Monthly 40, 461-464, August 1 1919
- ²⁹ Williamson Quoted by Holloway ¹⁰

THE PREPARATION OF NONPYROGENIC INFUSION AND OTHER INTRAVENOUS FLUIDS BY ADSORPTIVE FILTRATION*

REPORT OF 42 MONTHS' TRIAL

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PART I—BIOLOGIC ASPECTS

IN 1937, there was reported from this laboratory a method of preparing intravenous fluids based on a new principle^{1, 2} As pointed out in that report, it was Siebert's^{3, 4} extension of Hort and Penfold's⁵ work which laid the foundation for the various methods of preparing intravenous fluids at present practiced in commercial houses and hospitals Even the method described by Rademaker^{6, 7} and the more recent and mechanically ingenious elaboration by Walter,^{8, 9, 10} stem from Siebert's original principle The principle, however, suffers from a critical weakness in the assumption that if the water used in the manufacture of the fluids is pyrogen-free, then the resulting mixture must also be pyrogen-free But should the water become contaminated, say as a result of failure to clean the still, or should pyrogen be present in the chemicals used in making the solutions, the lack of provision for its removal is a notable disadvantage of the method It is, in fact, the lack of security behind the old working principle which impels manufacturers to test their intravenous fluids on the rabbit Unfortunately, not even this precaution has entirely eliminated the occurrence of pyrogenic reactions As pointed out in a previous communication,¹¹ this failure is perhaps due to the inadequacy of the test doses in use

That chemicals occasionally are contaminated with pyrogen has not heretofore entered into consideration In previous papers¹² we have reported on the pyrogenicity of samples of inulin as they have come fresh from the manufacturer

Table I shows the effect on test animals of samples of sodium chloride, of dextrose, and of sodium citrate, all "commercially" and "technically pure," which had been made into solutions with nonpyrogenic water and tested immediately after the containers had been opened The sodium chloride sample was the more reactive of two found pyrogenic in a test of 38 samples, an incidence of slightly more than 7 per cent The dextrose was the most reactive of four positive samples of 32 tested, an incidence of 14 per cent, and the sodium citrate was the most reactive of four of 18 tested samples, an incidence of over 22 per cent It may also be mentioned that sodium citrate

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PREPARATION OF INFUSION FLUIDS

is usually more heavily contaminated than dextrose which, in turn, is usually more heavily contaminated than sodium chloride. Because of the fact that test animals injected with such large doses of sodium citrate are liable to die in cardiac arrest, perhaps as a result of the blood calcium being thrown out of ionization, it is necessary to add an equivalent dose of calcium chloride to the sodium citrate test solution before it is injected.

TABLE I
EFFECT OF VARIOUS COMMERCIAL SOLUTIONS
Test Dose Gm

Exper No	Chemicals	Vol Cc	Animal Used	Weight Kg	Temp Rise Deg F	Leukocyte Count Change $\times 1000$
1	Sodium chloride	4 50	Rabbit	3	1 2	
2	Sodium chloride	12 1500	Dog	15	2 0	—5 7
3	Dextrose	7 5 150	Rabbit	3	2 0	
4	Dextrose	75 1500	Dog	15	2 4	—9 4
5	Sodium citrate*	0 28 11 5	Rabbit	3	2 2	
6	Sodium citrate*	2 8 115	Dog	15	2 8	—8 2

*These dosages were calculated on the bases that the maximum dose of sodium citrate given to a 60-Kg man is 5.6 Gm (3 liters of blood), and that the rabbit is approximately three times and the dog six times less sensitive to pyrogen than man. An equivalent amount of nonpyrogenic calcium chloride was added to each sodium citrate solution.

The chemicals in these cases were perhaps contaminated by pyrogen in the process of manufacture. Nonpyrogenic chemicals even in the "dry" state can, however, become pyrogenic on standing under unsterile conditions, as has been found by Smith¹³ to be the case with inulin, and by us with dextrose, sodium citrate and heparin. Apparently the better medium the chemical is for bacterial growth, the more easily it becomes pyrogenic. Humidity and a warm environmental temperature seem to accelerate pyrogen production, probably by acceleration of bacterial growth. Among aerial contaminants, Co Tui and Schiff^{14, 9} have found *B. proteus vulgaris* and *B. subtilis* fairly prolific pyrogen producers. In the light of these findings, therefore, the assumption that to guard against the occurrence of pyrogenic reactions it is necessary only to keep the water pyrogen-free can be costly as well as unsafe. The problem will perhaps become increasingly acute with the increasing use of blood and plasma transfusions.

The adsorptive filtration method of preparing intravenous fluids differs from the older method in that it is based on the principle of filtering the resulting mixture of chemicals and distilled water through specially prepared compressed asbestos pads proved to remove pyrogen. This method is efficacious not only for infusion fluids but for all crystalloidal intravenous medications. With colloidal substances such as sera and gum acacia, however, it is ineffective. The method has been in experimental use on the New York University Surgical Division of the Bellevue Hospital continuously since July, 1937 except for an intermission of 16 months. It is the purpose of the present communication to summarize the results of the experiment as well as to describe the practical method of manufacture which has been evolved.

The practical difficulties encountered in the course of this work may be briefly discussed since they are difficulties which many hospitals and similar institutions which undertake the manufacture of their own infusion fluids will have to face

1 The first problem was the establishment of the criterion of pyrogenicity. With fluids which are frankly pyrogenic, this is an easy matter since the symptom-complex of the pyrogenic reaction is a familiar one. The difficulty was with fluids containing a borderline dose of pyrogen, which would elicit only a slight temperature rise easily missed in the four-hour routine ward temperature readings but might, when administered in doses two or three times larger than the usual one, give rise to a fairly severe reaction.

It was therefore, necessary during the first six months of this experimental period to subject the fluids made to animal tests, using the rabbit and the dog, according to the technic described elsewhere.¹¹ If the fluids were found nonpyrogenic according to the tests, they were then released for ward use. The temperature readings of all patients receiving the fluid were taken hourly for four hours, both during and after the administration of the fluid. In this way transient temperature rises could be detected.

2 The second problem was the elimination of contamination from external sources, such as the rubber tubings, glass connections and needles used in the dispensing set. Originally, the latter were sterilized in the ward instrument sterilizers in common with contaminated pus basins and surgical instruments. The occurrence of four reactions on patients in the first three weeks of this period led to tests of the water from the sterilizer. Ten and 15 cc samples of this water gave unmistakable reactions in both rabbits and dogs. This result led to the institution of a method of washing, packing and sterilizing the dispensing sets which will be described in a later section of this paper.

3 A third difficulty was the presence of a yellowish-brown coloration in the solutions after they had been autoclaved. This was first thought to be due to caramelization but has been attributed by Krno¹⁵ to the production of levulinic acid.¹⁰ In our preparation two factors were found responsible for the coloration: (a) The asbestos pads originally used were made for the filtration of fluids which did not have to be autoclaved. They imparted some principle to the filtrate which caused the formation of this coloration on heating. The adoption of a pad specially prepared for infusion fluid use has eliminated this factor, and (b) the second factor was overheating of the solution. This occurred when, after sterilization, the autoclave pressure was permitted to sink so fast that the fluid inside the flasks began to boil over. The film of fluid on the inner wall of the neck of the flasks evaporated and the residue became browned, imparting the coloration to the rest of the solution. The remedy to this was obviously to lower the autoclave pressure so slowly that no boiling over took place.

4 The fourth and most serious difficulty was the presence of shreds and particles in the filtrate. While the injection of solutions containing these particles into numerous experimental animals caused no detectable symptoms,

their presence was none the less objectionable. It was because of this difficulty that the use of these fluids was suspended for 16 months in 1938 and the first part of 1939, until a manufacturer could be found who would cooperate in devising means of eliminating these particles. Jena filters, Chamberland and Berkefeld filters were interposed at the outlet of the asbestos filter without avail. Finally, the difficulty was overcome by both improving the quality of the filter pad and interposing an aloxite fiber eliminator between the asbestos filter and the collecting bottle.

5. Standardization of filter pads. The compressed asbestos pads, as now prepared for our use by the Ertel Engineering Corp., are calibrated with regard to two properties: (a) The speed of filtration, and (b) degree of pyrogen retentiveness.

Speed of Filtration—This is controlled by three factors: The filtering pressure applied, the filtering area, and the composition of the pad. The filtering pressure is safest at 12 lbs., and the filtering area is limited by the size of filter practicable in hospitals. Our present filter takes pads of 12 inches, with an actual filtering area of 29.5 cm. in diameter. The pads are made of asbestos and pulp. The more asbestos used, the greater the pyrogen retentiveness, but the slower the filtration rate. The interplay of these two factors, therefore, determines not only the rate of filtration but also the efficiency of the pads to remove pyrogen. The pad now in use has a delivery volume of two liters every 2.5 minutes. A six-hour filtration would, thus, yield 288 liters, which would be more than enough to meet the daily requirements of a fairly large hospital. Hospitals using larger amounts of fluid may enlarge the filtering area of the filter by the method to be described later or install two such filters.

Pyrogen Retentiveness of the Filter Pads—The ability of these pads to remove pyrogen was shown in a previous work¹⁶ to be due to adsorption and not to sieving. This means that the property can be exhausted. It is, therefore, necessary so to standardize the pads that they are not only uniform but also possess such a margin of safety in pyrogen retentiveness that they remove the maximum amount of pyrogen which can occur in the distilled waters and the chemicals in use.

In order to calibrate the pads in this respect it was necessary to secure a sample of pyrogen and use it as a standard. The pyrogen used in this work was isolated from the cell-free Berkefeld filtrate of the supernatant portion of concentrated stock suspension of typhoid vaccine (1 cc. = 88 billion cells). From seven liters of this suspension, four grams of the substance was yielded. The method of isolation as well as the chemical and biologic aspects of this substance will be reported elsewhere. It is necessary, however, to state that the substance is still in the crude stage, containing six per cent nitrogen, which on further purification has been reduced to 1.6 per cent. The biologic (pyrogenic) potency of this crude sample, called "pyrogen-A" has been determined on rabbits, dogs, and men. Table II shows the effect of different doses of this preparation. If the minimum effective dose (MED) is arbitrary

trarily defined as that dose, per kilo body-weight, which on intravenous injection will cause a temperature rise of 0.8° to 1.0°F , the MED in rabbits is 0.1 gamma, in dogs, 0.4 gamma, and 0.03 gamma in men. The reason for using this crude substance as a standard instead of the more purified substance is that the process of purification is so tedious that it may be a long time before enough of the pure substance can be available for this purpose. In any case, the biologic calibration of "pyrogen-A" makes it unnecessary to wait for the pure preparation.

TABLE II
EFFECT OF DOSES OF PYROGEN-A IN RABBITS, DOGS AND MEN

Subject	Weight Kg	Dose per Kg	Temp Change Deg F	Leukocyte Count Change $\times 1000$
Rabbit 1	3.0	0.12	0.8	
Rabbit 2	2.5	0.12	1.0	
Rabbit 3	3.0	0.12	0.9	
Rabbit 4	3.0	2.0	3.5	
Dog 1	15.0	0.3	1.0	-6.1
Dog 2	16.0	0.3	1.1	-5.5
Dog 3	15.5	0.3	0.8	
Dog 4	16.0	2.0	3.2	-10.2
Man 1	52.0	0.04	1.2	
Man 2	64.0	0.04	0.9	
Man 3	72.0	0.04	1.1	
Man 4	70.5	2.0	5.0	

Process of Calibrating the Pads—One milligram of "pyrogen-A" (1000 gammas) is weighed out on a sensitive analytic balance and dissolved in 100 cc of pyrogen-free distilled water. Ten cubic centimeters of this solution contains 10 gammas of pyrogen. Amounts of from five cubic centimeters up, in multiples of five, are filtered through test pads of a convenient size mounted in convenient filters. The filtrates are then tested in both rabbits and dogs. Table III shows the protocols of some of these tests.

TABLE III
CALIBRATION OF FILTER PADS

Experimental Animal	Weight Kg	Prefiltrate Cc	Total Dose Pyrogen in Prefiltrate Gamma	Temp Change Deg F	Leukocyte Count Change $\times 1000$
Rabbit 1	2.5	30	300	-2	
Dog 1	16.0	30	300	+1	-2
Rabbit 2	3.0	35	350	+2	
Dog 2	15.0	35	350	25	-3
Rabbit 3	3.0	40	400	+15	
Dog 3	15.5	40	400	+1	+1
Rabbit 4	2.5	45	450	+4	
Dog 4	16.5	45	450	+2	-8
Rabbit 5	3.0	50	500	+4	
Dog 5	15.5	50	500	+8	-1.2

It will be seen from Table III that the pad removes nearly 500 gammas of "pyrogen-A." Since the pad is 2.5 cm in diameter, it has a surface of 4.9 sq cm, and, therefore, each square centimeter removes over 100 gammas of "pyrogen-A." The filtering surface of the four large filter pads used in the hospital filter assembly are each 29.5 cm in diameter, making a total filtering area of 2734 sq cm. The amount of pyrogen removable by the entire filter

assembly is approximately 273,400 *gammas*. Since about 140 *gammas* are required to cause a temperature rise of 5.6° F in an average man of 70 kilos, this filtering area will remove about 1953 such doses.

When applied to solutions of sodium chloride or dextrose in distilled water this range of safety is more than ample as the amount of pyrogen contained in any combination of these three substances in the usual dose is tenuous and, further, the filter-pad assembly is made to deliver not more than 288 liters with each filtration. The case of sodium citrate requires special consideration. As shown in Table I, gram for gram, the contamination of pyrogen in sodium citrate is heavier. This, however, is more than offset by the fact that the dose of sodium citrate used per 500 cc of blood is usually in the neighborhood of 1875 mg in 75 cc of water. This, by weight, is only about one-fifth of the dose of sodium chloride in one liter of physiologic salt solution and less than one-twenty-seventh of the dose of one liter of 5 per cent dextrose solution. Therefore, in making sodium citrate solutions, it is only necessary to use two filter pads and restrict the manufacture to not more than 300 doses.

These calculations are admittedly based on biologic effects, and assume that pyrogen from sources other than the typhoid bacilli have the same potency per unit-weight as typhoid pyrogen. This assumption has no direct experimental basis at present. The only justification for applying the figures derived from "pyrogen-A" to the pyrogenic substances found in these fluids, whose exact source is unknown, is that they have so far held true in the samples whose pyrogenic content was roughly determined by the biologic test, then filtered through asbestos pads of the required area and then retested and found negative for pyrogen. In the absence of more exact knowledge, this approximate correspondence for the present can be used as a rough working principle. This method of pretesting before filtration may be used for any intravenous material whose maximum pyrogenic content has not been as thoroughly studied as have those of dextrose, sodium chloride, and sodium citrate.

RESULTS OF 42 MONTHS' TRIAL

During this experimental period, 3867 liters of intravenous fluids prepared by the nonpyrogenic method have been administered. They may be tabulated as follows:

No. of Administrations	Amount Given Liters	Total Given Liters
1815	1	1815
652	2	1304
123	3	492
64	4	256
<hr/> Totals 2654		<hr/> 3867 liters

In none of these was there a reaction. One patient who complained of a chilly sensation after receiving 1000 cc did not have a temperature rise. It

is clear that if any pyrogen was present in the solutions, it was in such minute amounts as to be below the MED even in three to four liters

PART II—MECHANICAL ASPECTS

The parts which comprise the entire filter assembly may now be enumerated and the more important items described. The filtering portion of the assembly is diagrammatically represented in Figure 1. It consists of a compressed nitrogen or air tank, A, which furnishes filtration pressure, the reservoir, B, which holds the prefiltered mixture, the filter itself, C, the aloxite fiber eliminator, D, and the collecting flask, E.

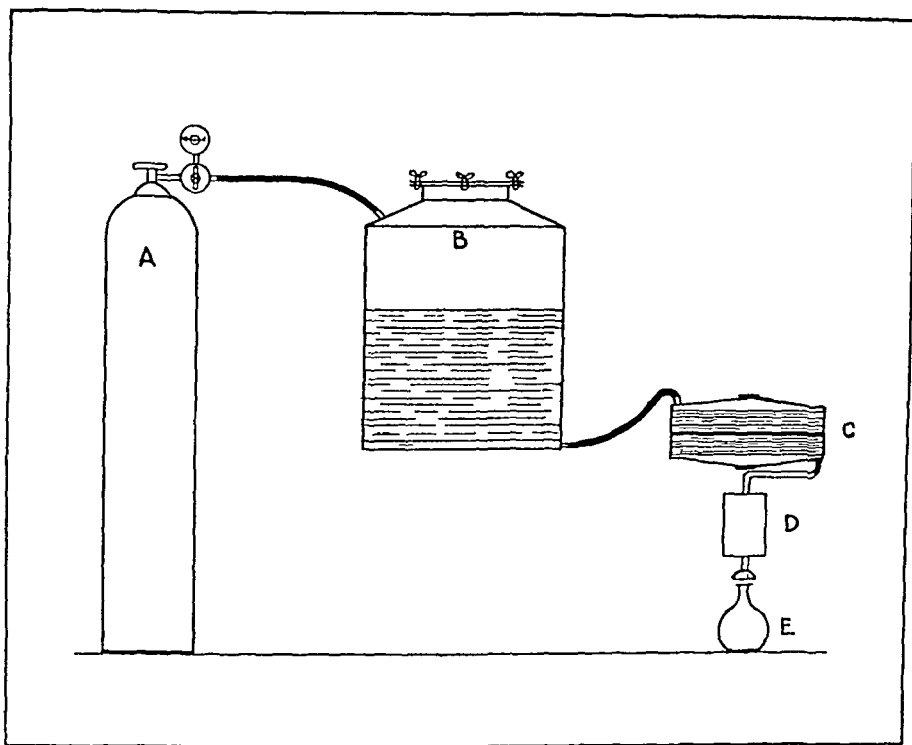


FIG 1

The reservoir, usually of 250 liter capacity, is made of stainless steel, and may be equipped with an electric stirrer.

Figure 2 illustrates the essential parts of the filter as well as the path taken by the solution passing through it. It may be seen that each filter pad is held between two perforated Monel metal plates or frames, the three forming a pad-frame unit. Two such units form a compartment. The fluid flows from the solution inlet, A, into a conduit system, B, which splits it into two streams. One stream filters through one pad downward and the other upward to meet in the collecting chamber, C, situated between the two pad-frames. From C the solution is conducted into the second compartment to have the process repeated, after which the conjoint stream from the second collecting chamber, D, passes through the fiber eliminator into the collecting flask. Both the latter are to be described in a subsequent section.

Since provision is made in the present filter to accommodate two additional compartments, the filter has a still wider range of usefulness than has been calculated. Any one of the three factors—capacity, speed of filtration, or retentiveness—can be increased two-fold by this doubling of the filtration area. The stream in this case would be split in four instead of two as in the filter illustrated in Figure 2.

Figure 3 is a photograph of the filter ensemble. A is the spindle with which the pads are loaded and unloaded and the filtering system rendered watertight. B is the filtering system, C is the pressure gauge, D the housing for the aloxite fiber eliminator, and E the outlet. The self-autoclav-

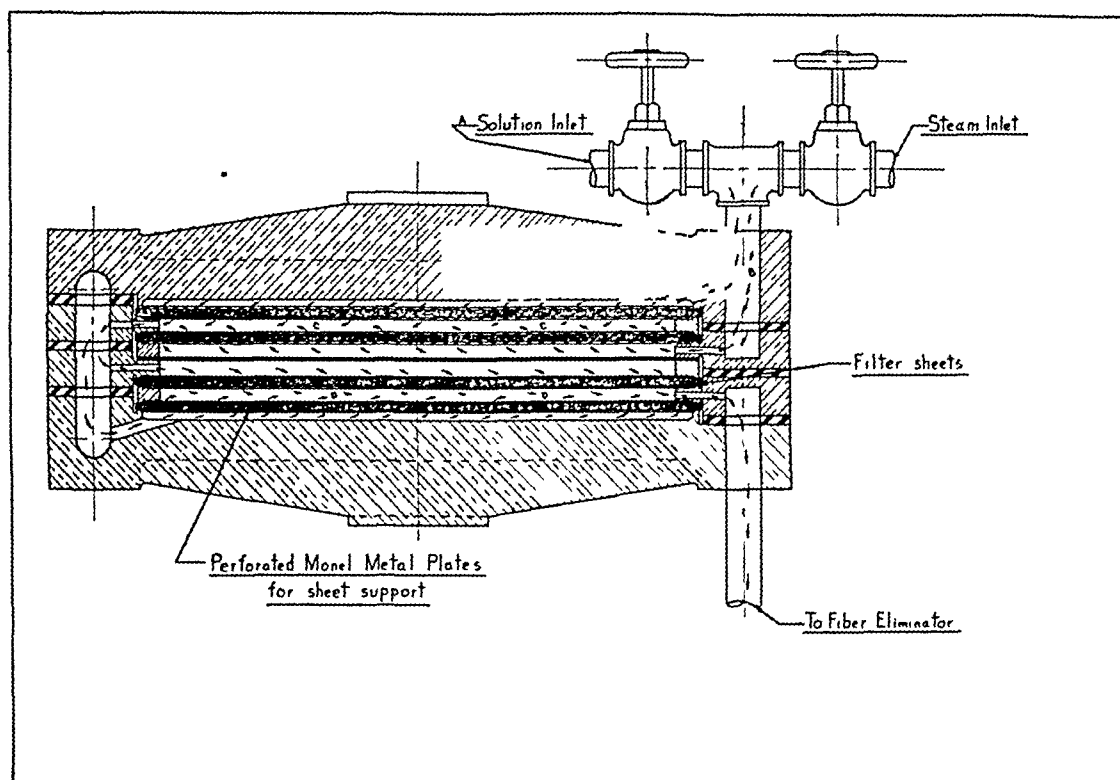


FIG. 2

ing system, F, consists of a steam generator in which the source of steam used is pyrogen-free distilled water. It may be heated electrically, by gas, by house-steam, or by an oil burner. The steam generated is led into the interior of the filter by the flexible hose, G. The course of the steam through the filter is identical with that of the fluid which follows it and whose course has been described in the foregoing paragraph.

The aloxite fiber eliminator is a thick, finely porous filter made of carborundum. Because of its composition it is sturdy and may be heated to a temperature high enough to destroy any pyrogen which may have developed in the interstices of the stone.

The dispensing part of this system, mainly the collecting and storing flasks and accessories, is essentially the same as that described by Walter^{8, 9, 10}. It is the most satisfactory one available at present, made to withstand hard

usage and in three years of use has suffered the minimum amount of breakage. It has, however, the slight inconvenience of having too many parts.

Figure 4 illustrates the part of this system which consists of A, pyrex flasks of specially rugged construction of one to two liters capacity, preferably graduated, B, a one-hole rubber bushing to fit the flask, C, a special stainless steel stopper with a partially grooved stem, D, a two-way vent tube for the administration of the fluids and for the admission of air into the flasks to displace the fluids.

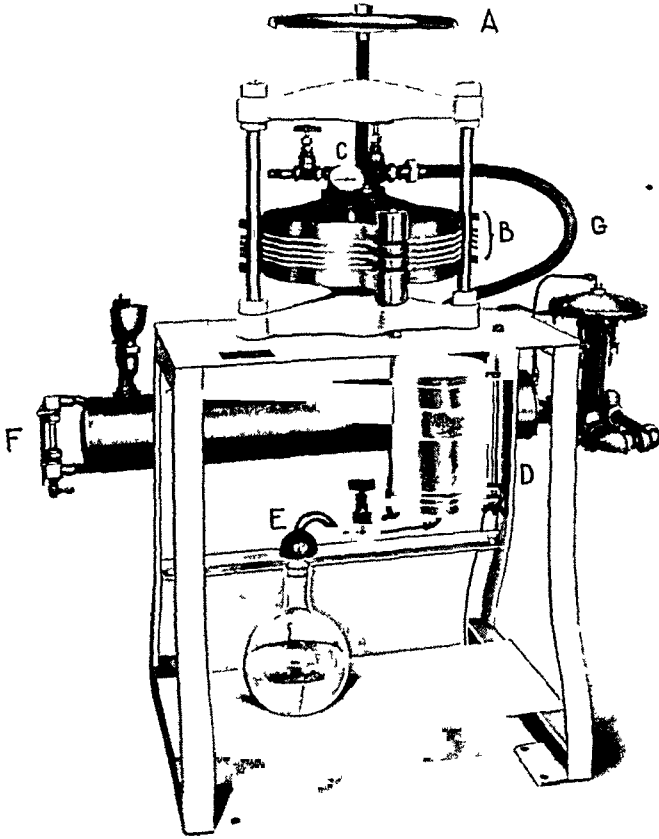


FIG 3

The bushing, B, is of special rubber which can stand 500 sterilizations without shrinking. It is provided with a hole in the center for the insertion of the two-way vent tube when fluid is being administered, and for the insertion of the steel stopper when the flask is not in use. The stopper is provided with a partially grooved stem which is fitted partly into the hole of the bushing while sterilization takes place. The groove allows equalization of inside pressure with outside pressure. When sterilization is completed the stem of the stopper is pushed all the way in, as in E, the umbrella of the stopper serving as an hermetic seal for the rubber bushing.

The original Fenwal-tube is short so that the flask end is submerged in the fluid when the flask is inverted for administration. There are two objec-

PREPARATION OF INFUSION FLUIDS

tions to this feature First, when the infusion is being given, the air which enters the flask to displace the fluid has to be bubbled through the fluid This, in effect, means the washing of 1000 to 2000 cc of unsterile air in the infusion fluid Bacteriologic cultures of ten samples of fluid subjected to this kind of air-washing gave three positive cultures By the simple device of

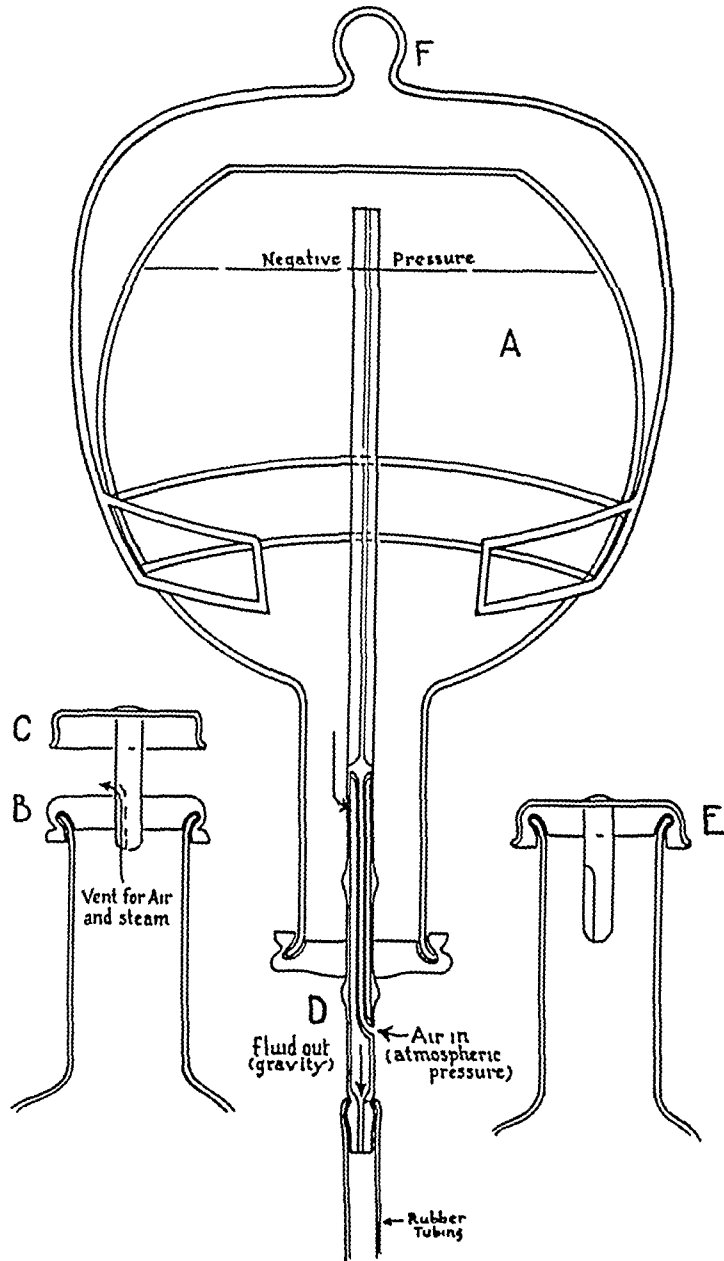


FIG 4

lengthening the tube so that the flask end extends above the surface of the fluid when the flask is inverted, this washing effect is avoided

No positive cultures were found in ten fluids subjected to this system of air displacement If it is desired to admit absolutely sterile air into the flask, the air vent may be modified in such a way as to accommodate a small sterile Berkefeld candle This was originally used by us but later discontinued because of inconvenience

The second objection to the short original Fenwal-vent-tube is that unless special care is taken, the fluid is as liable to flow through the air vent as through the fluid vent

The split ring bracket, F, is simply a wire basket for suspending the flask in an inverted position when the flask is in use

Some reference must be made to the still which delivers distilled water for making the solutions. Since the still is the heart of all other processes, much emphasis has been laid on it. While it is our opinion that the undue concentration on the still has lulled to rest suspicion of other possible sources of pyrogen, we believe that the still must be cleaned periodically so that it adds no pyrogen to the distilled water to lower the factor of safety of the filter. Moreover, it must be large enough to deliver the necessary amount of distilled water to be used for cleansing as well as to make the solutions themselves. A still that delivers 10 gallons of water per hour (40 liters), will be sufficient to meet the needs of the average hospital. The periodic cleaning also does away with incrustations which lower the output of the still.

CARE OF THE PARTS

The Reservoir The reservoir when new must be rinsed first with soap and water and then copiously with distilled water. Subsequent care after every use consists in rinsing it out thoroughly with distilled water and then drying it.

The Filter When new, the conduit system of the filter is rinsed thoroughly with distilled water. Thereafter, the same rinsing process is repeated after each use.

The Alomite Fiber Eliminator After every use, the surface of the stone fiber eliminator is simply flushed thoroughly in order to wash away the particles and shreds which may be caught on its surface. After washing, it is placed in an electric oven at a temperature of 120° C for one hour to dry. This temperature sterilizes the stone so that pyrogen production within the interstices of the stone is halted.

Fenwal-Flasks, etc The initial cleaning and subsequent care of the Fenwal-flasks, rubber bushings, steel cages, and the modified vent tube have been described by Walter and need no extended treatment here. Suffice it to say, that the flasks are washed and brushed with hot soapsuds and rinsed first in tap and then in distilled water until the walls run homogeneously clear. The same treatment should be applied to the other glassware, namely the vent tube and the drip as well as to the steel stopper. An occasional treatment of the glassware with a cleaning mixture of 1.5 per cent solution of sodium dichromate in concentrated sulfuric acid may have to be resorted to in order to get rid of spots in the glassware difficult to eliminate otherwise. The rubber bushings when new are first scrubbed with soap and water until no further powdery substance is given off, then rinsed with

distilled water. The rubber tubings when new are likewise rinsed well with hot soapsuds and then with distilled water. Immediately after each washing the rubber tubings, the vent tubes, the drip and the needles are wrapped and packed in a convenient container. We have used for this purpose a specially constructed copper cylinder, one foot long and $2\frac{1}{2}$ inches in diameter, provided with a detachable cap as well as holes in the wall to allow penetration of the steam in the autoclave. After sterilization, the holes are closed by a special sliding device and the set stored for future use.

Preparation for Filtration The flasks without the rubber bushings in place are sterilized in the hospital autoclave. The rubber bushings and the steel stoppers are also sterilized but separately from the flasks.

The filter with pads mounted on the frames is sterilized by its own self-autoclave for 30 minutes at 18 pounds pressure. After that it is allowed to cool to a temperature convenient for handling.

The solution is mixed in the reservoir. The reservoir is then connected, on the one hand, with the nitrogen tank and, on the other hand, with the inlet of the filter. The collecting and storing flask is placed at the outflow tube of the filter and filtration is begun by turning on the gas gradually to 12 pounds. After discarding the first four liters, the flasks are then filled one by one.

After collection, the flasks are partially stoppered with the stainless steel stopper in such a way that the groove in the stem of the stopper allows communication of the inside of the flask with the outside (Fig. 4). The flasks are then put into the autoclave and sterilized at 250°F for 30 minutes. After sterilization, special care is taken to have the pressure in the autoclave gradually diminished so as not to cause boiling. The stem of the steel stopper may then be pushed home, in which case a partial vacuum is created as the solution cools. This partial vacuum, which helps retain the stopper in place and causes a water-hammer effect when the bottom of the flask is struck with the fist, may be used to indicate whether the stopper is leaking after storage.

After the flask is sealed, it is stored until needed.

Just before administering the fluid, the steel stopper is removed from the flask with a rocking and unscrewing motion. The flask end of the two-way vent tube is now inserted through the hole in the rubber bushing to the point where one of the two dilations on the glass tube just slips into the flask beyond the rubber bushing. The flask is inverted, placed in the ring bracket, and the infusion started.

Calculation of Costs This method requires an initial equipment which may be divided into two parts, an irreducible item which consists of the reservoir and the filter, and an item which can be expanded according to need, namely, the flasks and their accessories. The rubber tubings and drip and needles do not enter into consideration here as they will have to be used in any case. The irreducible equipment costs about \$1000. If the cost of the flasks for initial use is set at \$600 and to this is added part-time labor of \$50 a month, which can be expanded into full-time labor as the need arises

the total may be set at \$2200. Any hospital which expends this amount of money a year for infusion fluids will not incur a loss, even in the first year, by adopting this system. Beyond the first year the savings are substantial, the larger the amount of fluids used, the more substantial the savings, since the only items of expense will be the cost of replacements, material and labor.

But the savings are not the entire consideration. The safety from pyrogenic reactions in intravenous medication, especially in blood and plasma banks, should be the major consideration, particularly during war times. Instances are known of tens of liters of blood and plasma which have had to be discarded because the sodium citrate used was pyrogenic. This type of saving has not entered into the above calculation but may be the major item.

SUMMARY AND CONCLUSIONS

1. Methods of intravenous fluid manufacture which depend only upon the purity of distilled water used have no provision for dealing with pyrogen should this substance be present in the final mixture and, therefore, do not entirely eliminate pyrogenic reactions.

2. Chemicals have been shown to be occasionally contaminated with pyrogen.

3. The adsorptive filtration method of preparing assuredly nonpyrogenic fluids, described five years ago, has been developed into a practicable and convenient method for hospital use.

4. The compressed asbestos filter pads, around which this method is built, have been calibrated for speed of filtration and pyrogen retentiveness. The factor of safety is shown to be more than ample for the most exacting use in the manufacture of physiologic salt, dextrose, and sodium citrate solutions.

5. The uniformly nonpyrogenic results of 42 months' use of fluids manufactured according to this method are reported.

6. The mechanical aspects of the method are described.

7. The method not only eliminates pyrogenic reactions but is also more economical than the use of commercial fluids.

The authors wish to acknowledge their grateful thanks to Dr. Edward M. Berneker, Commissioner of Hospitals, to Commissioner Albert Pleydell and to Mr. A. M. Moore of the Department of Purchase, City of New York, for their encouragement and cooperation in furnishing the equipment for the completion of this work, to Dr. William F. Jacobs, Medical Superintendent of Bellevue Hospital, for the privilege of installing the experimental filter in the Bellevue Hospital, to Mr. Francis X. Dealy, of the Ertel Engineering Corp. of New York, for his cooperation in the mechanical phases of the problem, and to Dr. Wilfred Ruggiero, Messrs. Arthur Yates, Angelo Benaglia, and Milton Schrift for their constructive suggestions, to Dr. Ralph S. Muckensius, of the Bureau of Laboratories, City of New York, to Lederle Laboratories, Inc., and to E. R. Squibb & Co. we are indebted to for supplies of the stock suspension of typhoid bacilli.

REFERENCES

- ¹ Co. Tui, McCloskey, K. L., Schrift, M., and Yates, A. L. A New Method of Preparing Infusion Fluids. *J. A. M. A.*, 109, 250, 1937.
- ² *Idem*. A New Method of Preparing Nonpyrogenic Intravenous Infusion Fluids. *Ibid.*

- on Removal of Pyrogen by Adsorptive Filtration ANNALS OF SURGERY, 106, 1089-1094, December, 1937
- ³ Siebert, F B, Fever-producing Substance Found in some Distilled Waters Am Jour Physiol, 67, 90, 1923
- ⁴ *Idem* Cause of many Febrile Reactions following Intravenous Injections Am Jour Physiol, 71, 621, 1925
- ⁵ Hort, E C, and Penfold, W J The Dangers of Saline Injections Brit Med Jour 2, 1589, December 16, 1911
- ⁶ Rademaker, L Cause and Elimination of Reactions after Intravenous Infusions ANNALS OF SURGERY, 92, 195, 1930
- ⁷ *Idem* Reactions after Intravenous Infusions Further Report on their Elimination Surg, Gynec and Obstet, 56, 956, 1933
- ⁸ Walter, C W Economical Intravenous Therapy J A M A, 104, 1688, 1935
- ⁹ *Idem* Preparation of Safe Intravenous Solutions Surg, Gynec and Obstet, 63, 643, 1936
- ¹⁰ *Idem* The Relation of Proper Preparation of Solutions for Intravenous Therapy to Febrile Reactions ANNALS OF SURGERY, 112, 603, 1940
- ¹¹ Co Tui and Schift, M H A Tentative Test for Pyrogen in Infusion Fluids Proc Soc Exper Biol and Med, 49, 320-323, 1942
- ¹² Co Tui, Schift, M H, McCloskey, K L, and Yates, A L Filtration Studies on Pyrogenic Inulin Proc Soc Exper Biol and Med, 35, 227-230, March, 1937
- ¹³ Smith, H W Personal communication
- ¹⁴ Co Tui and Schift, M H Production of Pyrogen by some Bacteria J Lab and Clin Med, 27, 569-575, 1942
- ¹⁵ Krno Private communication quoted by Walter ¹⁰
- ¹⁶ Co Tui, McCloskey, K L, Schift, M H, and Yates, A L Filtration Studies on Reactive Infusion Fluids Proc Soc Exper Biol and Med, 38, 297-300, 1936

A SIMPLE METHOD OF PLASMA PROTEIN ESTIMATION

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A KNOWLEDGE of the plasma protein level is desirable in all surgical cases. It is an absolute necessity in many surgical emergencies. Therefore, there is general interest in any means by which the blood plasma level may be quickly estimated.

Very frequently it is imperative to know whether or not the patient's plasma proteins have fallen below a given point. The exact plasma protein level is often unimportant. We merely want to know if the protein is about normal, less than normal, or in the dangerous range of five Gm or less per 100 cc of plasma. A variation of a few tenths of a Gm makes little difference. There often may be this much variation in the individual patient.

The means here suggested by which this estimation may be carried out is not new. We have borrowed liberally from others^{1, 2, 3, 4} and have merely reapplied certain previously reported principles to suit the present needs.

The method depends upon the relationship between specific gravity and protein content of a given plasma. This is applied by using tubes containing solutions of varying specific gravities. The specific gravities are adjusted so that they will equal given protein plasma levels. Therefore, when a drop of plasma is placed in the test solution, it will sink if it contains more protein than that represented in the test tube. Likewise, it will float if it contains less.

Specifically, we have made test solutions containing xylene and bromobenzene⁵. Using approximately 75 per cent of the former solution, bromobenzene was added until the correct specific gravity was obtained. This was determined by testing a portion of the mixture with a drop of potassium sulfate test solution having the desired specific gravity.

In the tests here described arbitrary specific gravities were selected. These were chosen so that they would have specific gravities corresponding with blood plasmas of 5.0, 5.8, and 6.5 Gm per 100 cc, respectively. The specific gravity values were obtained from Weech's formula⁴.

It is simpler for the average laboratory to use serum rather than plasma in these tests. Therefore, the amount of plasma fibrinogen was subtracted from the values given above. The usual value of fibrinogen is 0.27 Gm per 100 cc⁶. Then, for example, to obtain the specific gravity of blood plasma having 6.5 Gm per 100 cc, when using serum for the test, 0.27 Gm were subtracted from 6.5 Gm. The result is 6.23 Gm. The specific gravity corresponding to this protein content is 1.0253, when figured by Weech's formula or taken from Scudder's tables⁷.

Three such specific gravities were arbitrarily chosen and solutions were made of xylene and bromobenzene to correspond with these specific gravities. As noted, this was done by means of test solutions of potassium sulfate. These test solutions were titrated against the usual falling-drop apparatus in the laboratory. After the desired specific gravities were obtained, the potassium sulfate solutions were then used to titrate the specific gravities of the xylene-bromobenzene solutions. This latter operation was done by taking samples of the mixture in which xylene made about 75 per cent. Xylene or bromobenzene were then added cautiously, until a drop of the potassium sulfate test solution remained suspended half way in the small test tube sample. With the tubes thus carefully adjusted they were ready for trial with the unknown blood serum.

The values selected were as follows

Tube No

(1) 5.0 Gm — 0.27 Gm = 4.73 Gm = sp gr 1.0209

(2) 5.8 Gm — 0.27 Gm = 5.53 Gm = sp gr 1.0231

(3) 6.5 Gm — 0.27 Gm = 6.23 Gm = sp gr 1.0253

From the foregoing it will be noted that the tests are run on serum, but the results are given roughly in Gm of *plasma* protein per 100 cc.

Therefore, when the determination is run, a droplet of serum from the patient's clotted blood is allowed to fall into each of the three test tubes. If the serum contains less protein than that indicated on the tube, the serum droplet will float. If it contains more, it will sink.

Of course, the particular specific gravities may be altered to suit any individual requirement. The specific gravities used here seem to cover amply the needs of the usual surgical case. For instance, any blood which shows a plasma protein less than five Gm (serum floats in this tube) indicates that the case is extremely critical, requiring emergency measures. If the serum sinks in the five-Gm tube but floats in the 5.8-Gm tube, the plasma protein must be between these levels. This would indicate a serious situation, but one not demanding the immediate attention cited in the first example. Likewise, we have argued that blood containing more than 6.5 Gm per 100 cc of plasma needs no protein therapy. This at least holds true for the surgical patient.

It is essential that the xylene-bromobenzene mixture be maintained at a known definite temperature during the tests. In the present instance they were titrated at 25° C (77° F). Therefore the tests on the unknown plasma must be run at this temperature. This is necessary since the specific gravity of the xylene-bromobenzene solution changes rapidly with any change in temperature. A variation of 1° C from 25° C makes little difference. However, a 5° C variation produces an error which makes the test quite useless. The temperature is easily maintained by means of a glass of water and an ordinary thermometer. The three tubes are placed into this simple water bath for one or two minutes before running the test. It is more accurate to keep them immersed while dropping the serum into them.

If plasma is used instead of serum, a substration of 0.3 Gm (approximate) must be made from the final result

The three tubes (Fig 1) are used but once and then discarded. They are cheap and become inaccurate with repeated use. So that there will be

no confusion in identifying the three tubes, a red dye was added to color the solutions. For this, Sudan IV was employed. The solution in the 6.5-gram tube was stained red, that in the 5.8-gram tube was stained pink, and the 5-gram tube was left colorless.

The tubes were closed with cork stoppers. After closure the corked ends were dipped in a thick celluloid-acetone solution. This proved satisfactory for at least a few months. How much longer it would prevent evaporation is not known. Rubber corks were purposely avoided because of the action of xylene on rubber.

Caution. Several points of caution should be mentioned in this brief description. First of all, the specific gravities of the solutions must be extremely accurate. Carelessness in titrating the solutions may produce errors of nearly one gram in the final result.

All tests must be run at the temperature used in titrating the original xylene-bromobenzene

solutions. A variation of one degree centigrade from this original temperature cannot be exceeded.

Small test tubes (2 cc) were used for economy. This necessitated care and practice in getting the droplet of serum to fall into the solution without touching the sides of the tube. A small pipette giving small drops was an aid in this step.

Readings must be made in the first half minute or minute after the drop of serum is introduced into the solution. Occasionally, if this is not done, enough diffusion of electrolyte takes place so that a false reading is obtained.

Tubes must be opened just before the test. They are inexpensive and therefore, can be discarded after

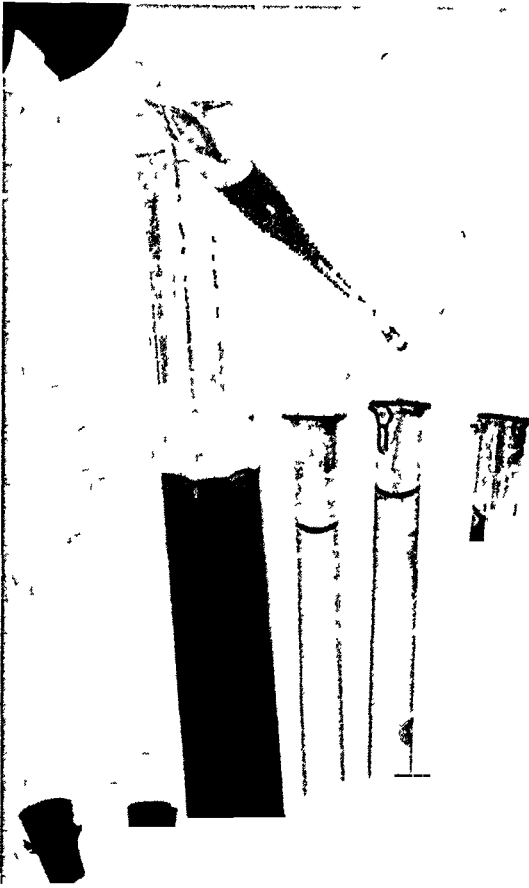


FIG 1—Estimation of Plasma Protein. A drop of serum from the large test tube on the left has just been placed in the center small tube. This tube has a specific gravity equal to plasma protein of 5.8 Gm per 100 cc. Since the drop is sinking to the bottom of the tube, the serum must contain protein in excess of 5.8 Gm per 100 cc.

Lastly, the limits of this test for plasma protein must be fully realized. It is a rough determination but possibly a life-saving one in an emergency.

SUMMARY

- 1 A simple test for the rapid estimation of plasma protein is outlined.
- 2 The test depends upon the utilization of solutions of known specific gravity. Into these are placed droplets of serum from the blood to be tested. This estimation of the specific gravity indicates roughly the amount of protein present.
- 3 The test is crude but accurate enough for the usual surgical patient.
- 4 This procedure is not suggested as a substitute for any of the methods of plasma protein determination now in use, such as the quantitative balance and volumetric pipette method, or the falling-drop method. It is suggested for use in the small hospital unit, for ships and units of the military forces where such tests are not now available. Here it might well be a life-saving guide in cases of severe burn trauma, or shock.

REFERENCES

- ¹ Barbour, H. G., and Hamilton, W. F. The Falling-Drop Method for Determining Specific Gravity. *Jour. Biol. Chem.*, **69**, 625, 1926.
- ² Moore, N. S., and Van Slyke, D. D. The Relationship between Plasma Specific Gravity, Plasma Protein Content and Edema in Nephritis. *Jour. Clin. Investigation*, **8**, 337, April, 1930.
- ³ Page, I. H., and Van Slyke, D. D. A Simple Test for Plasma Protein Contents below the Edema-producing Level. *J. A. M. A.*, **99**, 1344, October 15, 1932.
- ⁴ Weech, A. A., Reeves, E. B. and Goettsch, E. The Relationship between Specific Gravity and Protein Content in Plasma, Serum and Transudate from Dogs. *Jour. Biol. Chem.*, **113**, 167, 1936.
- ⁵ These chemicals were Eastman Kodak Company's No. 43 bromobenzene and T-275 M-xylene.
- ⁶ Best, C. H., and Taylor, N. B. *The Physiological Basis of Medical Practice*. Ed. 2, The Williams and Wilkins Co., Baltimore, 1940.
- ⁷ Scudder, J. *Shock*. J. B. Lippincott Co., Philadelphia, 1940.

OBSERVATIONS ON THE FAILURE OF HEPARIN TO INHIBIT THE CLOTTING OF BLOOD IN VITRO BY STAPHYLOCOCCI*

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IT IS WELL KNOWN that certain strains of staphylococci will produce the clotting of citrated plasma ^{1, 2, 3} These strains contain the so-called "coagulase factor" which is considered to be different from the toxin that produces the hemolysis and the tissue necrosis ⁴

Much,⁵ in 1908, showed that the anticoagulant hirudin did not inhibit the clotting of plasma by staphylococci Giatia⁶ also observed that both hirudin and peptone would not inhibit the clotting of plasma Cobra venom and chloroal-fast pink likewise do not prevent the clotting of plasma by staphylococci ⁴ Walton⁴ has recently demonstrated that heparin has no effect on the clotting of citrated plasma as produced by a staphylococcal Berkefeld-V filtrate

In the present experiment heparin has been studied to determine its effect on the clotting of both whole blood and citrated plasma by staphylococci Some of these strains contained the coagulase factor Observations are also included on the effect of staphylococcus toxin on the clotting of blood and citrated plasma

Materials and Methods—Cultures of the following staphylococci were used in these studies

- Strain A — *Staphylococcus aureus* — Stock culture
- B — *Staphylococcus aureus* — Otitis media
- C — *Staphylococcus albus* — Otitis media
- D — *Staphylococcus aureus* — Otitis media
- E — *Staphylococcus albus* — Skin of arm—No lesions
- F — *Staphylococcus citreus* — Skin of arms—No lesions
- G — *Staphylococcus aureus* — Stock culture

All of these strains were nonhemolytic when grown on the surface of blood agar plates made with human blood The organisms were grown in nutrient broth for 4 to 24 hours before they were added to either citrated plasma or whole blood The amount of the inoculum was 0.1 cc

Citrated human blood and citrated human plasma were obtained from the blood bank It was usually the blood from syphilitic patients The concentration of sodium citrate was 0.4 per cent Rabbits' blood was obtained by bleeding the animals from the heart The concentration of sodium citrate in this blood was 0.77 per cent The rabbit plasma contained the same quantity of citrate as the blood

* Aided by grants from John and Mary R Markle Foundation, and the University of Tennessee

In some of the experiments four cubic centimeters of either blood or plasma was used while in others the plasma was diluted three parts of plasma and one of saline. In each experiment the volume of each of the constituents was kept constant. Test tubes 15 x 12 cm. were used. They were usually kept for two hours in the water bath at 37.5° C, and then in the incubator for varying periods up to 48 hours.

The defibrinated blood was obtained from both man and rabbit. It was defibrinated with glass beads. The staphylococcus toxin was prepared by Lederle laboratories. Two one-hundredths (0.02) of a cubic centimeter of this toxin produced complete hemolysis of 20 cubic centimeters of a 10 per cent suspension of rabbits' red cells. The toxin was detoxified by heating it for five hours in a water bath at 56° C. One cubic centimeter of this heated toxin did not lyse the above concentration of rabbits' cells.

Heparin* was used in these experiments both in the presence of sodium citrate and as the only anticoagulant. When used as the latter, one part of heparin was added to three of rabbit blood. The quantity of heparin added to the citrated plasma and the citrated blood varied in the different experiments. The exact quantity is given in the protocols. One cubic centimeter of this preparation contained 10 mg. of the sodium salt of heparin.

In this experiment where suspension of staphylococci were used the organisms were grown on the surface of agar slants for 48 hours. They were carefully washed from the agar surface and again washed four times in large amounts of saline. The bacteria were then suspended in saline. The following dilutions of the saline suspension of staphylococci were used: Undiluted, 1-10 and 1-100.

Experimental Studies—Observations on the Clotting of Citrated Blood and Plasma by the Strains of Staphylococci Used in this Experiment. The results obtained following the inoculation of the tubes of both the citrated blood and the citrated plasma with the seven strains of staphylococci are given in Table I. The rate at which the clot formed varied in the rabbit and the

TABLE I
CLOTTING OF BLOOD BY STAPHYLOCOCCI
Rabbit Citrated Blood* Human Citrated Blood

Strain of Staphylococcus	Time in which Clotting Occurred									
	30 Mins	60 Mins	2 Hrs	7 Hrs	22 Hrs	30 Mins	60 Mins	2 Hrs	7 Hrs	22 Hrs
A	0†	+	+	+	0‡	0	0	+	+	+
B	0	0	+	+	+	0	0	0	0	?
C	0	0	0	0	0	0	0	0	0	0
D	+	+	+	+	+	0	+	+	+	+
E	0	0	0	0	0	0	0	0	0	0
F	0	0	0	0	0	0	0	0	0	0
G	0	+	+	+	?	0	?	+	+	+

* 3.0 cc. of the blood + 1.0 cc. of saline and 0.1 cc. of broth culture used in each tube. Water bath 37.5° C for 3 hours and then put into incubator at 37.5° C.

† 0 = no clot, ? = questionable clot, + = clot.

‡ Clots frequently dissolve after varying periods of time.

* This preparation of heparin is Liquaemin. It was supplied by Roche-Organon Inc., Nutley, New Jersey.

human blood. There was also some variation in the time of clotting of the different batches of citrated plasma. The time in which clotting occurred was likewise influenced by both the age and the size of the inoculum. The clotting occurred more rapidly when 0.1 cc. of a 24-hours' broth culture was used than it did when an equal quantity of a five-hour growth was added.

The length of time in which the clot persisted following formation varied in the rabbit and the human blood. In the latter blood and also in citrated human plasma the clot frequently remained for 48 hours at which time the tubes were discarded. The clot in the rabbits' blood began to liquefy after approximately six hours, and sometimes after 24 hours the blood had returned to a fluid state. Hemolysis began to occur in the rabbits' blood shortly after the clot developed. Extensive hemolysis was present within 24 hours. It appeared to us that the rate of liquefaction of the clot in the rabbits' blood increased with the increase in the degree of hemolysis. The strains of staphylococci that failed to produce clotting also did not lyse the red cells. Essentially no hemolysis occurred in the tubes containing the human blood.

Effect of Staphylococcus Toxin on the Clotting of Citrated Plasma. In the preceding experiment it was suggested that the clots were dissolved through the effect of the toxin liberated by the staphylococci. Tubes of citrated human plasma were inoculated with the strains of staphylococci that produced clotting. When a clot was well formed one cubic centimeter of staphylococcus toxin was added. This quantity of toxin produced no macroscopic changes in the clot during 48 hours of incubation at 37.5° C.

This observation was repeated with citrated rabbit plasma, since the rabbit cells were more susceptible to the hemolytic action of the toxin. Following the appearance of a clot in the rabbit plasma 0.5 cc. of staphylococcus toxin was added to a series of tubes. An equal amount of heated toxin was added to a second series for the control. The clot produced by some strains of the staphylococci was definitely decreased in size and appeared softer in consistency after 20 hours of incubation. Staphylococcus toxin apparently had no effect on the clots in human plasma.

Observations on the Rate of Formation of the Clots in Human Plasma. It appeared from the early observations in this experiment that both the age of the broth culture and the amount of growth influenced the rate of development of these clots. To study this further one of the strains of staphylococci (G) was grown on the surface of an agar slant. The organisms were washed and suspended in saline. One group of tubes containing four cubic centimeters of citrated human plasma were inoculated with 0.1 cc. of this suspension of organisms. A second series with a 1-10 dilution, and a third with a 1-100 dilution. The tubes inoculated with the concentrated suspension of organisms were clotted after three hours of incubation. Those inoculated with the 1-10 dilution were found clotted after 18 hours, while the set of tubes inoculated with the dilute suspension were clotted only after 48 hours.

These observations would suggest, therefore, that the clotting of citrated

human plasma results from either some substance or some change in the medium produced by growing staphylococci. The strains of staphylococci that produced the clotting of citrated blood and plasma when inoculated into tubes of defibrinated blood did not produce any clotting.

Effect of Heparin on the Clotting of Citrated Blood and Plasma by Staphylococci. It has been shown in these experiments that certain strains of staphylococci when added to citrated blood and citrated plasma will produce clotting. Since heparin is an anticoagulant its effect was studied on the formation of these clots by the different strains of staphylococci. One cubic centimeter of heparin (10 mg.) was put into each of four sets of tubes. Three cubic centimeters of citrated human blood was added to one set of tubes, a corresponding amount of citrated human plasma was added to the second set and an equal quantity of citrated rabbit blood was added to the third. Each tube was inoculated with 0.1 cc. of a broth culture of the seven strains of staphylococci. Clotting occurred in the tubes with the heparin the same as in the controls in which one cubic centimeter of saline was added.

To study further this phenomenon of clotting, rabbits' blood was obtained directly from the heart and it was put immediately into a flask with heparin (1 part heparin and 3 parts blood) and four cubic centimeters of this blood was then put into each of a group of test tubes. These tubes were inoculated with a broth culture of staphylococci. Clots formed in this blood in the presence of a 25 per cent concentration of heparin as readily as they did in citrated rabbit blood in which saline was substituted for the heparin. It was evident, therefore, from these observations that the failure of heparin to inhibit the clotting of both citrated plasma and citrated blood in the presence of certain strains of staphylococci was not the result of the neutralization of the heparin by the sodium citrate.

DISCUSSION—Certain strains of staphylococci when inoculated into citrated human plasma and citrated rabbit blood produced a clot. This clotting of citrated blood was similar to the clotting of citrated plasma by the "so-called" coagulase producing strains of staphylococci. Heparin when added to both citrated blood and citrated plasma in a 25 per cent concentration had no inhibitory effect on the formation of the clot. Other anticoagulants such as, hirudin, cobra venom and chlorazol-pink likewise have no inhibitory action on the formation of clots by staphylococci in citrated plasma^{4, 5, 6}.

It was necessary for fibrinogen to be present in the blood for clotting to occur when the medium was inoculated with staphylococci. This was experimentally shown by the failure of clotting to occur in defibrinated blood from both man and rabbit. Some change occurred in the blood in the presence of growing staphylococci to produce this clot. The rapidity in which the clot formed was influenced by the size of the inoculum. Rabbits' citrated blood and plasma were clotted more rapidly by the staphylococci used in this study than the citrated human blood and the human plasma. Citrated human plasma from different individuals also clot apparently at different rates by the same strains of staphylococci.

The substance responsible for this clotting of blood and plasma was not present in the preparation of staphylococcus toxin used in this experiment. Walton⁴ observed that a Berkefeld-V filtrate of 2 to 14-day cultures was active in the clotting of citrated plasma. He tested the filtrate of ten strains of staphylococci, eight of which clotted before filtration, and found that none of them were active in the clotting of plasma. These observations suggest, therefore, that the filtrates from only certain strains of staphylococci can produce the clotting of citrated plasma. The dissolution of the clot in rabbits' blood, accompanied by hemolysis, suggested that this process of clotting and that of hemolysis were produced by different substances. Walton has stated that "the clotting principle is distinct from the toxin responsible for local inflammation and fixation."

The dissolution of the clot in rabbits' blood and plasma apparently occurred as the result of the effect of the toxin liberated by the growing staphylococci and also by the toxin present in the filtrate used in this study. The failure of any dissolution to occur in the clots in the human blood was interesting in view of the fact that human red cells were not lysed by the strains of staphylococci used in this study. Red blood cells from man are usually more resistant to the hemolytic action of staphylococci than rabbit red cells.⁷

It may be significant that heparin has no effect on the clotting of blood as produced by different strains of staphylococci. Heparin is now being used in conjunction with chemotherapeutic agents in the treatments of certain types of staphylococcal infections.⁸ If heparin acts similarly *in vivo* and *in vitro* its effect on thrombophlebitis may be expected to differ with the different types of staphylococci.

SUMMARY

The "coagulase" strains of staphylococci produce clotting of citrated blood from both man and rabbit.

The clot that is formed in rabbits' citrated blood by these strains of staphylococci gradually dissolves. This dissolution apparently results from the action of the toxin liberated by the growing bacteria on the clot.

Heparin in a 25 per cent concentration does not inhibit the clotting of blood as produced by the "coagulase" strains of staphylococci.

REFERENCES

- ¹ Loeb, L. The Influence of Certain Bacteria on the Coagulation of Blood. *Jour Med Research*, 10, 407, 1903.
- ² Chapman, George H., Conrad, Berens, and Merritt, H. Stiles. The Coagulation of Plasma by Staphylococci. *Jour Bact*, 41, 431, 1941.
- ³ Dienst, R. B. A Study of Recently Isolated Strains of Staphylococci and their Ability to Coagulate Human Plasma. *Jour of Lab and Clin Med*, 27, 663, 1942.
- ⁴ Walton, H. D. The Clotting of Plasma Through Staphylococci and their Products. *Jour Hygiene*, 35, 549, 1935.
- ⁵ Much, H. Über eine Vorstufe des Fibrinfermentes in Kulturen von Staphylokokkus aureus. *Biochem Ztschr Bd* 14, 143, 1908.
- ⁶ Gratia, A. Action coagulante du staphylocoque sur le plasma hirudine. *Compt rend Soc de biol*, 82, 1393, 1919.
- ⁷ Rigdon, R. H. Hemolysis Produced by Staphylococcus Colonies and Toxin on Agar Media Containing Various Animal Bloods. *Jour Lab and Clin Med*, 24, 1264, 1939.
- ⁸ Schall, LeRoy A. Treatment of Septic Thrombophlebitis of the Cavernous Sinus. *J A M A*, 117, 581, 1941.

DRAINAGE AND WOUND CLOSURE TECHNIQUE IN APPENDICITIS OPERATIONS

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DEATHS FROM APPENDICITIS throughout the United States continue to be appallingly high. Deaths from appendicitis in many of the large hospitals in the United States are extraordinarily low. This indicates that technique and experience are important. An appendicitis operation may be one of the easiest operations in surgery or one of the most difficult. Entirely too many operations for appendicitis are being performed in the United States by doctors who lack this skill in technique and experience.

Problems of wound closure depend a good deal on wound-making and the necessity for drainage. Incisions for appendicitis should be made as close to where the appendix is located as possible. The minimal amount of damage should be done to the abdominal wall. They should be made so that drainage when necessary will be effectual and as free from postoperative complications incidental to introduction of foreign body material into the peritoneal cavity as possible.

Variations in the situation of the appendix are well known. Recognition of where the appendix is situated (Fig 1) can be gained before operation to a considerable degree of accuracy by a careful study through (1) percussion tenderness carried out with an even degree of gentle pressure, (2) deeper graded finger-tip pressure, (3) rectal examination, and (4) the study of a plain roentgenogram of the abdomen which in a large number of cases, will show a characteristic gas shadow of the cecum and ascending colon.

The best incisions for acute appendicitis operations are illustrated in Figure 2. The McBurney incision is unquestionably the best incision unless there be some convincing reason otherwise. It can be made slightly high or slightly low. Where more exposure is needed especially toward the midline the Weir extension through the linea semilunaris into the rectus sheath, with retraction of the rectus toward the midline often makes a difficult operation relatively easy. In certain cases of doubt as to diagnosis especially if a resection of the right colon may be needed a transverse incision (Fig 2C) just above the iliac crest to just below the umbilicus is a good one. In certain cases where the diagnosis may be questionable or there is indication of a large pelvic abscess with extensions to the right and left iliac fossae a midline incision (Fig 2D) may be indicated. The so-called right rectus incision should be mentioned only to be condemned not only from the standpoint that drainage through such an incision creates a drainage tract with coils of small intestine on all sides but also because the drains are liable to injure the superior mesenteric vessel to the small intestine and the right colon. The posterior sheath and peritoneum of a right rectus

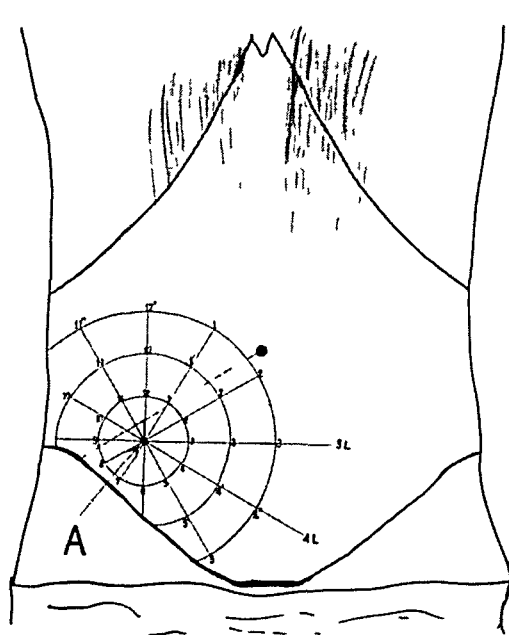


FIG 1

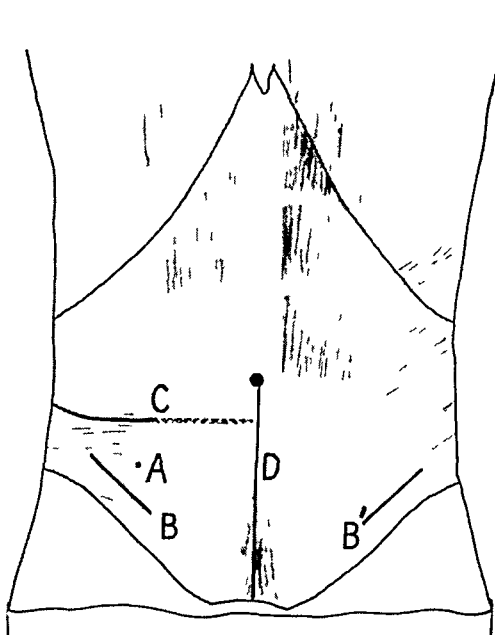


FIG 2

FIG 1—Use of the "clock dial" for convenience of description in appendicitis. McBurney's point one half inch below the junction of the outer thirds of a line from the umbilicus to the anterior superior spine, is used as a center. The numbers e.g. 12 12 12", at the intersection of the radiating lines with the circles are used for localization descriptive purposes. The outer circle reaches to the midline below the umbilicus. Points to the left of the midline have a capital L added.

In appendicitis records especially for anyone making an intensive study of the subject the "o'clock" method for precision in charting symptoms, physical signs, operative technic, and pathologic findings, has a number of rather obvious advantages.

INCISIONS

FIG 2—A. McBurney's point. One half inch below the junction of the outer and middle thirds of a line from the anterior superior spine to the umbilicus.

B. B. McBurney's incision. On the left side this incision is shown to be over the aponeurotic portion of the external oblique. On the right side, it is shown in relation to the internal oblique. At this level the internal oblique fibers are transverse. The transversalis muscle is transverse throughout, so that at this point direction of the two muscles is the same.

Common faults in making this incision are (1) the skin incision is made unnecessarily long. Skin stretches more than one anticipates after the deep fascia is cut, and (2) it is made too near the midline often in the linea semilunaris and the rectus sheath unintentionally. If drainage be required it is well in the great preponderance of cases to have the drains well away from the midline and small intestinal coils.

When convincing evidence of abnormal situation of the appendix exists, the incision can be made a little high or a little low, or a Weir extension into the rectus sheath made according to obvious demands.

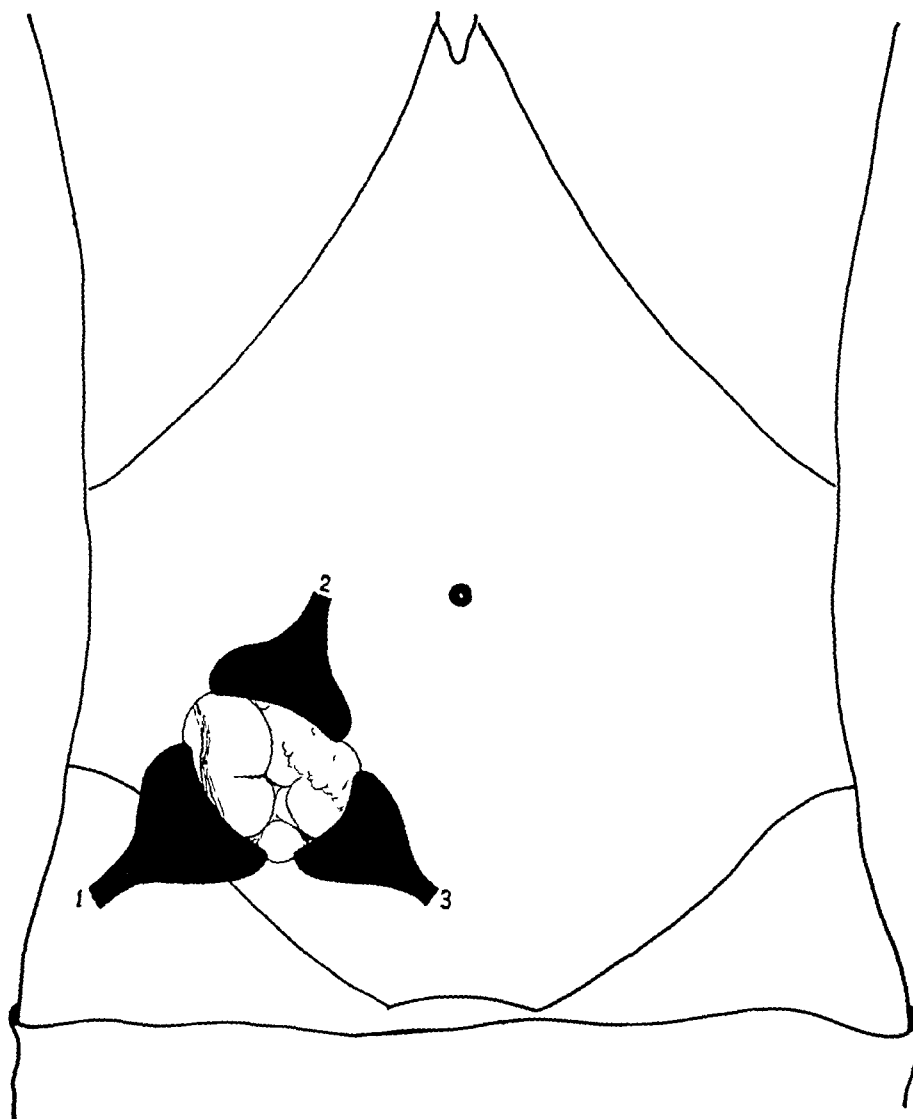
C. Transverse incision. Suited for cases where the cecum has not descended and the appendix is high or when the appendix is retro or laterocolic, or where a lesion that may require resection of the right colon is difficult to distinguish from appendicitis.

D. Midline incision. When accurate diagnosis is impossible the signs preeminently pelvic, or pelvic organ disease not unlikely, this incision gives the best exposure with the least disturbance to the highly specialized neuromuscular structures of the abdominal wall. It should be borne in mind however that where the cecum is in its normal iliac fossa position, and an inflamed appendix tip in the pelvis, the McBurney incision with or without the Weir extension, is the incision of choice.

One should differentiate between two associated factors in determining the incision best adapted for appendicectomy. First the site of the cecum, and second the site of the appendix itself. A preoperative roentgenogram may be of great assistance in determining the cecal site but the clinical signs may be of greater value in determining the site of the appendix. A cecum situated normally in the right iliac fossa may be associated with an appendix whose inflamed tip may be under the liver or deep in the pelvis. Easy access to the cecum helps appendix removal. Easy access to the appendix—especially its tip—also aids removal.

Thus a preoperative roentgenogram that almost always will show gas shadows indicating the site of the ascending colon and cecum coupled with the findings on clinical examination, may considerably help determine the best site for an incision that will provide best exposure for removal and least harmful site for accurate and adequate drainage. Such reasoning and forethought may save life. Indeed it is its lack that more often than we think may be the one determining factor that makes it impossible for a case to get well.

incision may be very difficult to close, especially if there be distention. Omental and intestinal adhesions to this imperfect closure occur, especially when this incision is made at the level of the umbilicus and below. The right rectus incision is responsible for a large number of postoperative intestinal



"THREE-POINT" RETRACTION FOR SIGHT

FIG. 3.—'Seeing the situation' should be the surgeon's first thought when the peritoneum is opened. A good exposure aids more than anything else in finding the appendix quickly and removing it with minimal harm. Two retractors may give a good view, but three are better. Delicacy, precision and using the eyes and head to guide the hand is priceless. The good surgeon is always a gentle man.

obstructions. It would be wise to do away with the right rectus incision in the middle and lower abdomen entirely.

After opening the peritoneum through a McBurney incision the first thing an operator should remember is to study his problem by sight. The practice of immediately putting one's finger through a small opening and searching for an inflamed appendix with the finger-tip and then making an effort to pull it out regardless of its pathologic condition is bad. Three-

point retraction (Fig 3) provides an excellent method for seeing, before doing. The cecum, or ascending colon, should first be looked for. They are recognized, of course, by means of longitudinal striae. Once found, these striae lead to the appendix. In making this search retraction should be outwards, because the cecum and ascending colon, lie usually along the lateral abdominal wall, posteriorly. The appendix stump should be inverted without ligation. It is well known that other methods are advocated by many, but they are not as good surgery.

It often takes much skill and experience to remove a badly infected appendix, especially with abscess formation. Much has been said recently about draining the abscess and leaving the appendix in. There are occasional cases where this is advisable. This is where skill and experience count. The proper thing to do is always to remove the appendix unless there is convincing evidence that it is wiser to leave it in. Where there is skill and experience, the appendix can practically always be removed, and if done carefully and accurately, it is much the better thing to do.

The reasons for drainage are not always too obvious, and the trite remark "when in doubt, drain," has a certain quality of value. In many cases, a careful history, as to the *length of time* serious infection, with likely spread into the mesentery and surrounding parts, enough to cause necrosis of tissues in the neighborhood, that cannot be removed, is of value. The writer recalls assisting the late Dr Joseph Blake, over 30 years ago. He removed a gangrenous appendix, and sucked out considerable real pus from the pelvis and peritoneal cavity, yet closed the wound. At that time the writer was amazed. The boy got well, without complications. The point was that the boy had felt apparently perfectly well only four hours previously. He had hardly had time to develop secondary necrosis in the tissues outside of the appendix. The necrotic tissue had been removed by the removal of the appendix, and in spite of the fact that the pus was almost creamy, the tissues, left behind, retained their nutrition adequately to care for the brief contamination they had been submitted to. Contamination precedes infection. Infection is dangerous. Infection that has had long enough time to make dead tissue is still more dangerous. Factors that contribute to infection, that leads to devitalization of tissues left behind, provide reasons for drainage. Long operations, much handling, many ligatures, colon-content contamination, foreign bodies, insecure inversion, exposure of retro-peritoneal tissues, that are far less able to care for infection than the peritoneum itself, evidences of mesenteric thrombosis with its associated devitalizing effects and true abscess formation, all of these, are reasons for drainage.

Useful principles and methods of drainage are indicated in Figures 4, 5, 6 and 7. Where there is little evidence of necessity for draining the peritoneal cavity, but where the infection has been considered a serious one, especially in stout people, and where resistance may have been impaired, drainage of the wall either to the peritoneum or to the aponeurosis is often safer than closure. There are times when a loosely packed cigarette

OPERATIVE TECHNIQUE IN APPENDICITIS

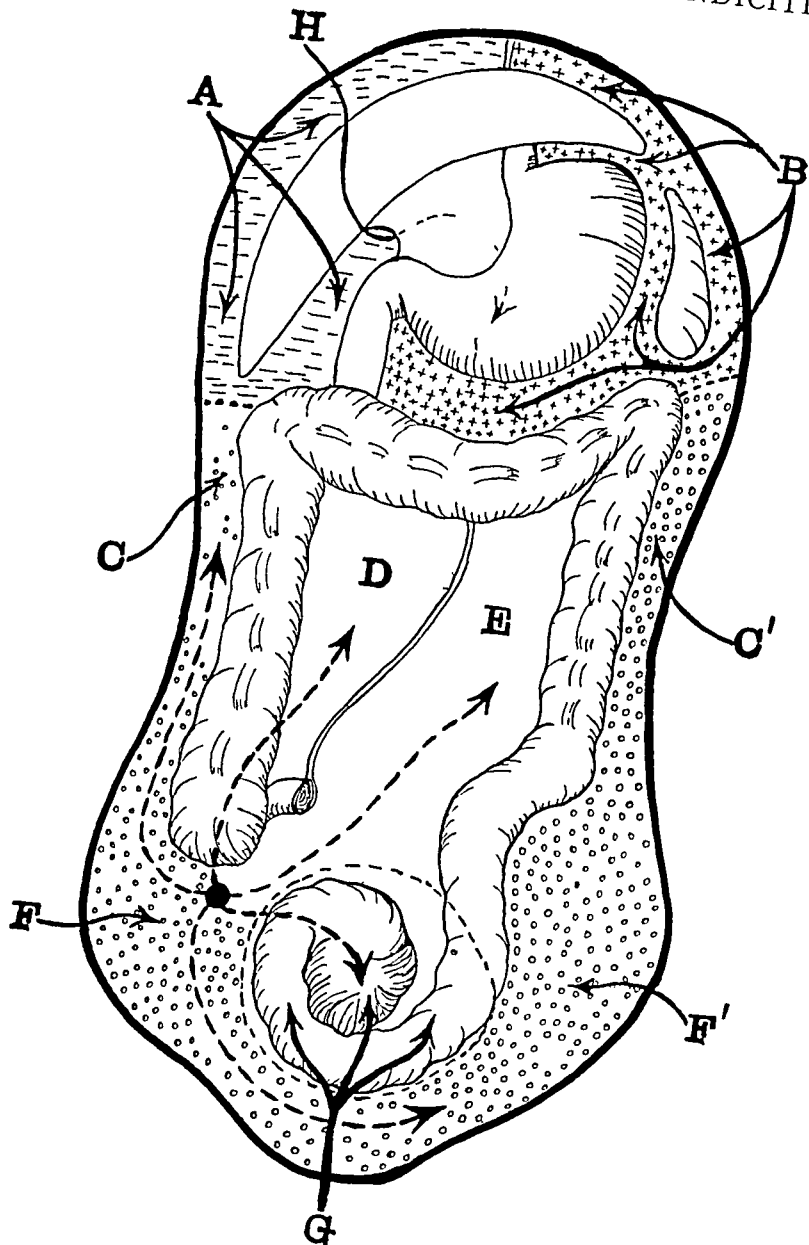


FIG 4—Schematic drawing (after Testut Traite' d'Anatomie Humaine) showing the principal pouches of the peritoneal cavity. The dotted lines indicate the routes along which infection from an inflamed appendix travels, largely according to the position of the appendix with reference to the cecum. Quite apart from these intraperitoneal extensions are the extraperitoneal when the appendix lies behind the cecum, ascending colon or ileocecal junctions. Such retroperitoneal infections toward kidney, pancreas, and along the great vascular routes are equally important and present serious problems.

One must understand these routes of infection dissemination in order to operate and drain intelligently, as well as appreciate the likely localization of, and approach to, secondary abscesses.

A Hepatic fossa. This includes the right subphrenic, and subhepatic abscesses.

B Gastric fossa. This is in front of the stomach, and includes the perisplenic and left subphrenic spaces.

C and C' Right and left parietocolic, or laterocolic spaces. These communicate with the hepatic and gastric spaces above and the right and left iliac fossae below.

D Right, mesenterocolic space. Infections from appendices in front of the ileocecal region—a relatively rare position—extend to the right of the mesentery, in contrast to

E Left, mesenterocolic space. Infections to this region are more common because of the relative frequency of appendices pointing toward the pelvis and in this direction (Fig 5).

F and F' Right and left iliac fossae. Most appendix abscesses of course are in the right iliac fossa. Extensions to the left iliac fossa from the pelvis in front of the rectum along the left leaf of the mesosigmoid are not uncommon.

G The pelvis. The rectum forms more of a dividing line in the pelvis than is generally appreciated. Abscesses on the right of the rectum may extend up and into the left mesenterocolic space.

H When the abscess has extended to in front of the rectum and toward its left side, the extension is to the left iliac fossa.

I The foramen of Winslow leading from the hepatic space into the lesser sac. Abscesses of the lesser sac from appendicitis are practically unknown.

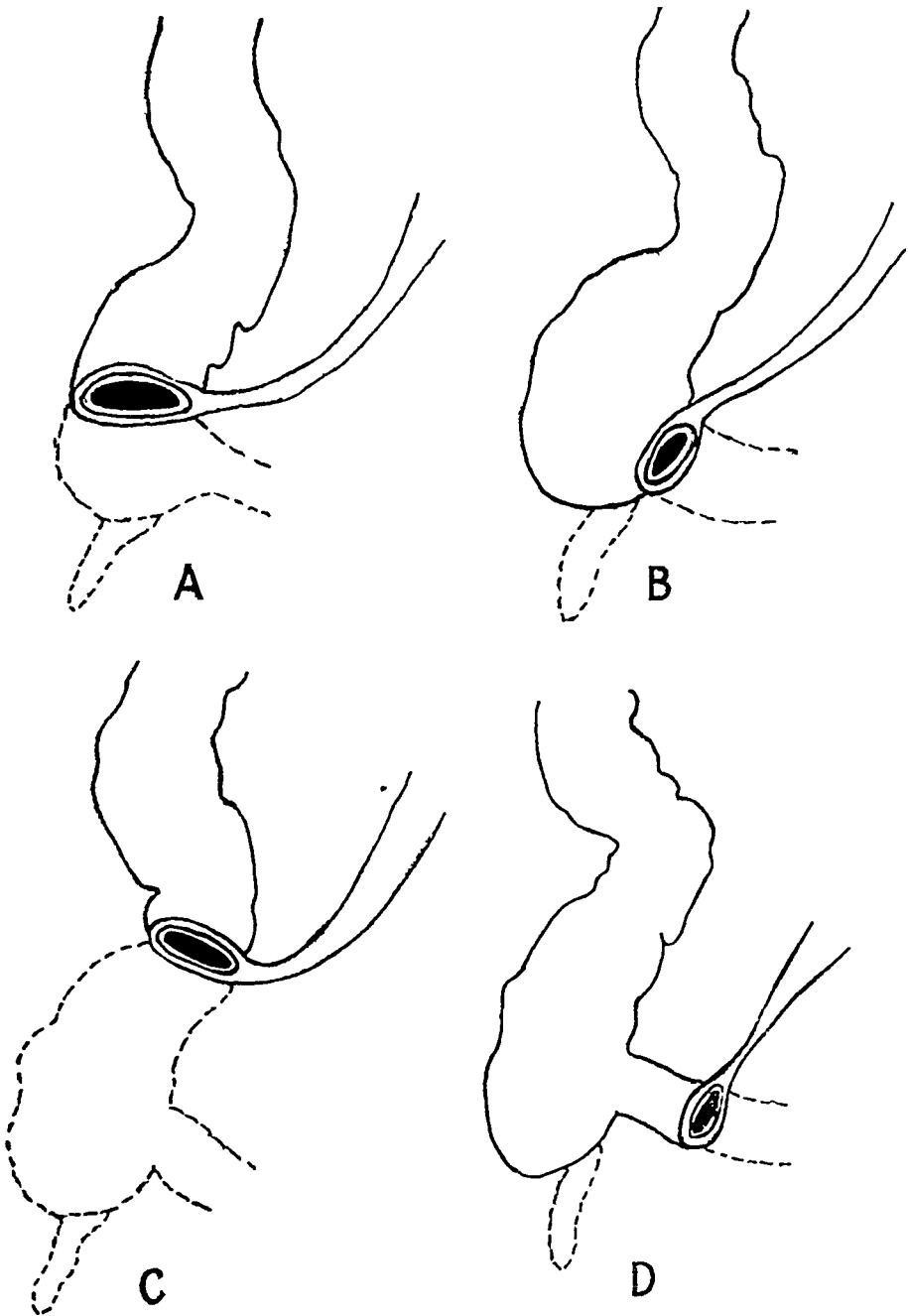


FIG. 5—Variations in the attachments of the lower pole of the mesentery (d'après Turnesco Traité d'Anatomie Humaine Testut)

- A Cecocolic junction This is the classical, normal arrangement
- B At ileocecal valve
- C Ascending colon
- D Terminal ileum

These variations especially A, B and C show how readily dissemination of infection to the pelvis and to the left mesenterocolic space (Fig. 4 E) can occur in the majority of cases. Of course, in the laterocolic, retrocolic and antecolic appendices this rule does not obtain.

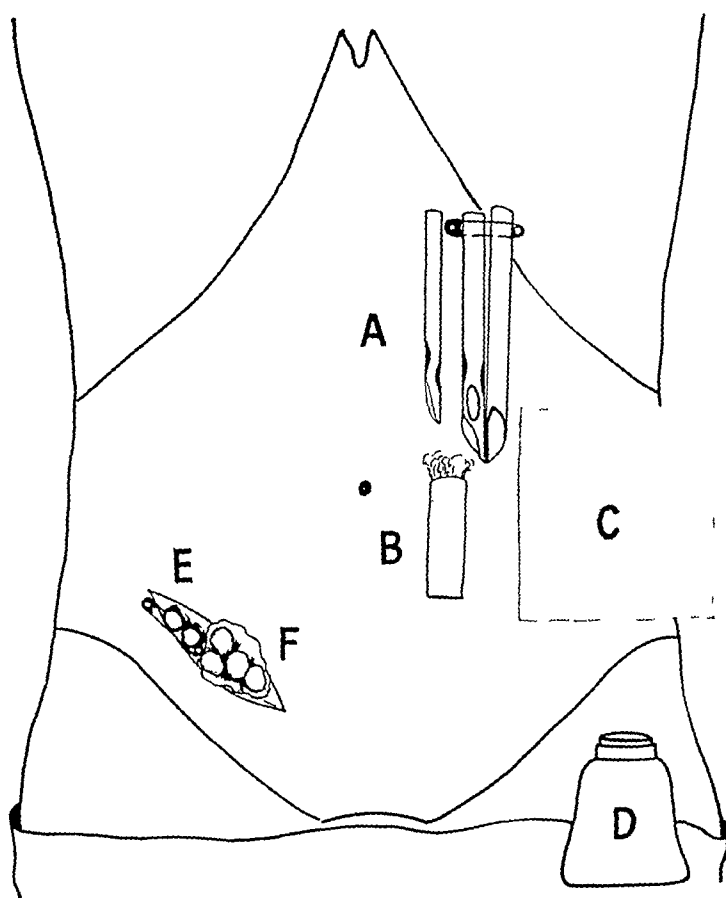


FIG. 6—Appendicitis with abscess drainage through a McBurney incision. How to drain and leave a "wide open" wound "closed" without suture.

A Fairly large, rubber tubes with soft walls. These are fenestrated and beveled, and used single or double. One limb of the double tube is cut a little longer than the fenestrated limb and left without holes. This can be used subsequently for irrigation purposes. A loosely packed piece of gauze tape can be used for a few hours in the fenestrated tube to prevent a blood clot from filling the tube. The inner ends of these tubes should be accurately placed, not necessarily to where purulent exudate is found, but where the tissues have been killed by the infection and slough has already occurred, or is expected, to occur. Early removal of such tubes is not to be expected. They must be left in long enough to maintain a tract until sequestration and separation of the dead sloughs from the living tissues is complete. Gently loosening them and cutting off their protruding ends, bit by bit making sure that their inner ends still reach the bottom of the sinus without causing undue pressure—letting them "shorten themselves"—is an art requiring judgment and experience.

B Cigarette drain. Gauze should not protrude from the inner end of this drain. It is not as good a drain as a tube. It is a "plug" and, as such, is useful in keeping wounds open, with the minimal risk of causing pressure necrosis. Where infection necrosis is minimal, when the length of time has been so brief as to make it seem unlikely that, though the appendix may be necrotic, the tissues left behind, after its removal, are not seriously devitalized, a cigarette drain may serve the purpose of maintaining the wound open for about 48 hours, with less likelihood of causing pressure necrosis than a tube. There are probably a certain number of cases where the proper use of tubes has been the determining factor in saving the patient's life and the use of cigarette drains inadequate. On the other hand, it should be clearly understood that the improper use of tubes can do just the opposite. It is the way in which they are used, nice precision and experience that count.

C A sheet of thin Chinr silk. This, fenestrated or not, is far preferable to gauze, when used against the tissues to keep the wound open yet prevent evisceration as the inner lining of a tampon. One or more short cigarette drains, used inside silk, make an excellent tampon and are easily removed or replaced without causing pain or hemorrhage.

D A salt shaker is employed for convenience in dusting the crystals of sulfanilamide, sulfathiazole or other medication, on or in the silk tampon, or in the wound.

E The tubes in place with a safety pin beneath which dressings can be placed to prevent them being pushed in further than intended.

F Four cigarette drains giving bulk to the tampon, inserted just through the peritoneum to maintain the unsutured wound wide open and prevent evisceration.



FIG. 7.—Drains and materials used for 'staple suture' wound closure

- A Small, large, soft single, and double rubber tubes
 B Silk containers filled with gauze. Crystals of sulfanilamide or sulfathiazole etc., can be smeared on the outside or put inside these containers and used as replacement drains in the sinuses after removal of the tube drains
 C Cigarette drains. Gauze does not protrude from their inner ends
 D A sheet of China silk to be used for tamponade
 E A sheet of sponge rubber. A roll of this wrapped in boric ointment gauze provides a good buffer on which to seat the shot fasteners on the skin surface bearing of the "staple" suture described under Fig. 8
 F Reverdin needle. This, or larger skin needles, are useful in placing "staple" sutures
 G Small cuticle clipper useful in making the split shot. Even better yet are pruning shears, one blade of which is sharp, the other flat
 H Strong silk sutures with split shot fasteners
 I A split shot held by a pair of pliers. An elastic band about the handles holds the shot in place before crushing

drain (Figs 6B and 7C) a short distance into the peritoneum, to be removed within 24 or 48 hours, may be advisable. In considering the serious infections, however, of the peritoneal cavity, soft rubber tubes (Figs 6A

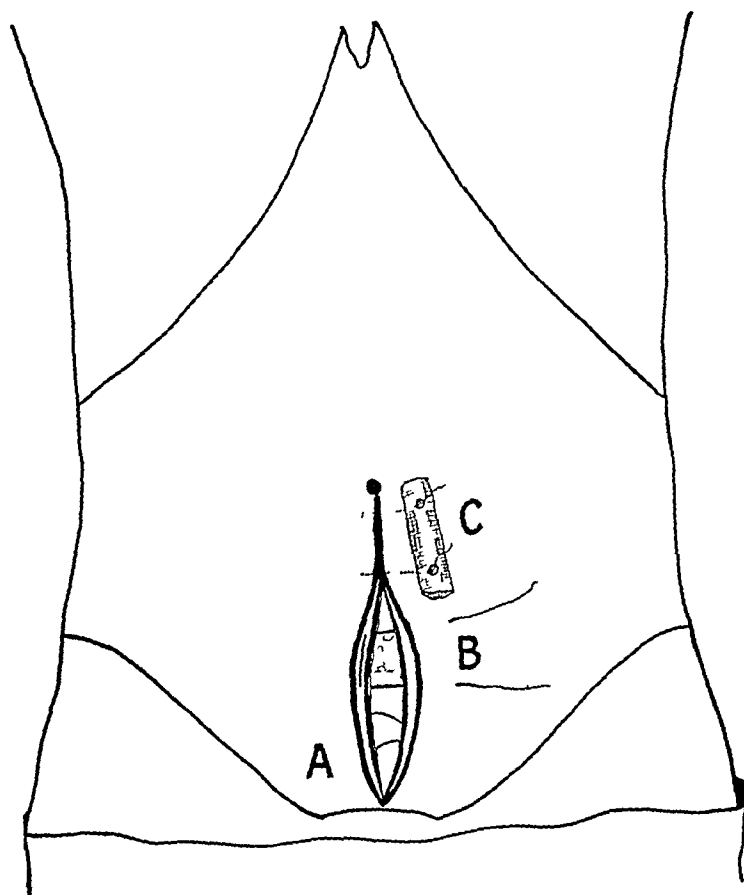


FIG 8—The "bolt", or "staple" type of suture for wound closure

A The lower part of a midline abdominal wound to be left open for drainage

B The suture. Strong silk passes through the skin on the left side through the anterior sheath and peritoneum, and often through the inner portion of the rectus, then through the peritoneum and anterior sheath on the right. The tough fibers of the anterior sheath (linea alba) if the incision has been carried slightly to the left of the midline is used to bear the burden of the strain. This, after all, is the one structure in this wound capable of doing so. Two or three centimeters away the suture is passed in reverse direction. This brings the opposing bearing on the skin surface.

C This shows the wound closed and a method for handling the skin surface bearing. A roll is made of sponge rubber wrapped in boric ointment gauze. The sutures are passed through this and fastened by split shot. Often the skin falls together in correct apposition so that sutures are unnecessary. In infected cases the subcutaneous tissues can be left open without weakening the closure.

From the standpoint of time consumed, simplicity, minimal strangulation of tissue, number of sutures, strength of closure, avoidance of wound infection, and the amount of "foreign body" material left in the wound, this method is best, in my experience.

and 7A) are the best. They provide a space in the depths of the peritoneal cavity comparable to the surface of the body into which exudate can immediately accumulate under minimal tension. For many years now, it has been recognized that closure of the wound about such drainage, where the infection has been a serious one and there has been much necrosis, is inadvisable. However, if the wound be not closed, evisceration may take place alongside

the tubes. A good way to prevent this is the use of a China silk tampon (Figs 6C, F and 7D, C) into which have been inserted cigarette drains packed with somewhat more than the usual amount of gauze that is not allowed to protrude from their inner ends. These give bulk and can be easily and painlessly removed in a few days because they do not stick. The silk tampon is subsequently removed with minimal disturbance to the tissues it comes in contact with, far less than if gauze were used.

The use of sulfanilamide, or sulfathiazole, and the newer similar drugs (Fig 6D) locally, has been pretty well proven of real value from the standpoint of their bacteriostatic effects. It can be dusted as a fine powder on the silk tampon (Fig 6F) described above, after the silk has been wet with salt solution, or directly into an abscess cavity or over the tissues of the wound in the abdominal wall. In similar fashion these drugs can be used on long, finger-like sacs made of silk and filled with gauze tape (Fig 7B) for subsequent dressings, especially after the tubes have been removed. Wounds treated this way are certainly free of foul-smelling "colon" pus and heal more rapidly and with less necrosis than heretofore.

The use of a tampon to prevent evisceration when it is desirable to have a small wound wide open, is usually adequate, even though distention occurs. This is not so in a larger wound such as in some midline wounds. Figures 8B, C and 7E, F, G, H, I, indicate the principles that make the "bolt-" or "staple-type" of suture reliable. This gives the strongest closure with the fewest sutures and least necrosis. The wound can be left wide open for drainage, or not. If used correctly, even the skin edges may be so nicely apposed as to need no sutures.

IMMEDIATE SKIN GRAFTING IN THE TREATMENT OF BURNS

A PRELIMINARY REPORT

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IN February, 1941, Mason¹ made a plea that burns be regarded as surgical wounds, and thought that results might be improved if the same principles used in treatment of other traumatic wounds be followed. These principles of cleansing, débridement, hemostasis, closure, and rest, are well known and generally accepted. Moreover, it is known that they hold only if wounds are cared for within a few hours following injury, preferably within six hours certainly not longer than 12 hours. It is probable that this simple view of burns has not previously obtained because of the wide extent of the injury and the poorly understood cause of the shock found in severe burns.

Without going into the various theories of shock production, it now seems probable that shock in burns is, for the most part, due to fluid loss from the burned surface, and into the tissues about and beneath the burn, this loss of fluid accounting for the decrease in circulating fluid and protein and relative increase in blood cells. With this better understanding of burn shock, it is now possible to more adequately control it by plasma administration guided by frequent hematocrit, and plasma protein determinations. In fact if the burn is seen soon, it is possible, within certain limits to forestall shock by replacing plasma as it is lost. It, therefore, becomes possible, in even extensive burns, to save patients whose injuries would formerly have caused death from shock within a few hours of the injury.

The extent of the wound and its treatment then becomes increasingly important, for we are now able to save patients with wounds of much greater surface-area. But with the partial solution of this problem another has appeared. These patients may be successfully carried through the initial shock period only to succumb as long as one to three months later. This late death is probably not entirely due to infection, although this is the generally accepted view. It may be that there is a loss from these extensive open wounds of necessary body constituents not as yet understood.

There are various facts which support this view. Extreme emaciation develops in these patients with large granulating surfaces and they may die in this stage even though infection seems minimal. This is illustrated by the following brief case report.

Case 1—S M H, No 167072, G S, white, male, age 35 received deep third-degree burns of the entire trunk and most of the upper extremities, and first- and second-degree burns of the face and hands. The area involved, as estimated by Berkow's charts was 55 per cent of the body surface. The burn occurred one to four hours before admission.

The exact time was not known as the man had been found in an alcoholic stupor on a burning davenport. He was in deep shock—B P 60/0, Hb 23.5 Gm, hematocrit 63.2. Within the next 64 hours he received 5800 cc of plasma and 7500 cc of saline intravenously before his blood pressure stabilized at 120/60. The burned areas were tanned but became grossly infected. On the ninth day he was started on tub baths in an attempt to remove necrotic tissue and control infection. The temperature chart showed continual improvement and the granulations became quite clean. In spite of this he became emaciated and very weak. He steadily lost weight and strength in spite of the fact that the lesions appeared cleaner. Many areas were perfectly healthy and pinch-grafting was started. During the fourth week he became irrational and delirious, with high fever, and a blood culture showed *B. aerogenes*, 260 colonies per cc. He expired on the 30th day.

We have observed that the fever curve of a patient comes down in step-like plateaus as a large granulating surface is covered at intervals.

Case 2—S M H, No 37348, H S, white, male, age 11, received a total third-degree burn of the left lower extremity from hip to ankle, a second-degree burn of the medial surface of the right lower leg from knee to ankle, first- and second-degree burns of the hands, and first-degree burns of the face. The total body area involved was estimated as 30 per cent. He was seen one hour after injury. He was not in shock—B P 110/68, hematocrit 59.9, Hb 16.5 Gm. The serious nature of the burn was not recognized by the house officer who saw him, and he was started on saline compresses, without intravenous therapy. Moderate shock developed and was controlled by plasma administration. He developed severe infection in the necrotic tissue. This was gradually controlled by saline compresses and saline tubs. It was 40 days before the necrotic tissue had separated and granulations enough appeared so that skin grafting could be considered. He was running a septic type of temperature, averaging about 39°C (102.2°F). About one-quarter of the left lower extremity was covered with split-thickness grafts. The temperature averaged 38.5°C (101°F) after this. Ten days later another quarter of the leg was covered, and immediately the temperature plateau fell to 38°C (100.4°F). Thirteen days after this, most of the remaining open half of the extremity was grafted, and the average temperature curve dramatically and promptly fell to 37.5°C (about 100°F).

This boy during his illness became extremely emaciated but survived and over a period of two to three months, gradually returned to normal.

It is common experience that there is improvement of the general condition of the patient if a large granulating surface is covered with homografts—even though these grafts, as is well known, persist only from two to six weeks.

It would seem then that if Mason's view, that a burn is a traumatic wound, is accepted, that treatment should be directed toward an attempt to secure primary healing. This, if possible, would eliminate these delayed deaths caused by the open wound. We believe that the various methods of local treatment of burns now in use do not meet this requirement.

Tanning—There are many agents used to produce an eschar over the burned surface. The one most commonly used is tannic acid. The objective of these agents has been stated as (1) To prevent fluid loss by sealing the surface, (2) to prevent the absorption of decomposition products of the dead tissue, (3) to provide a comfortable dressing which need not be changed, and (4) to prevent infection. From the standpoint of wound care, we have

never considered tanning to conform to the principles necessary for first-intention healing. In deep second-degree burns there is probably some destruction of viable epithelial remnants by the tanning. But the greatest violation of surgical principles by tanning is the locking-in of micro-organisms. Most tanned burns, in our experience, eventually become infected.

Local Treatment by Antiseptics—The production of an eschar by various dyes, designed to prevent the infection so commonly encountered in tannic acid treatment, has the same objections as tanning. Infection is usually not prevented.

Saline Baths or Compresses—This method is, perhaps, of the greatest use in the late treatment of extensive granulating areas. It has been employed in primary treatment of burns. It is of most use for burns of the hands and face. But in third-degree burns the end-result is a granulating wound which is frequently more or less infected. In our experience, it is quite arduous for an acutely ill patient, and must oftentimes be discontinued because of exhaustion. Its main advantage over tanning is that third-degree areas are ordinarily ready for grafting at a considerably earlier date.

The Closed Compression Dressing Method—This treatment is based on sound surgical principles. It is in essence the Orr-Triquetra treatment of compound fractures applied to burns. It was originated by Koch and Mason, and Mason¹ states that by this method the mortality rate in the Children's Wards, at Cook County Hospital, has been reduced from 10 to 3.9 per cent. In brief it consists in (1) Thorough soap cleansing (2) Débridement of loosened epidermis (3) The application of ointment-saturated gauze strips over the area (4) The application of a voluminous dressing, applied under moderate pressure (5) Leaving the dressing in place for 10 to 14 days.

We are in complete accord with this method, and believe it superior to any other now in use. It is ideal for first- and second-degree burns. Healing *per primam* usually occurs in two weeks. The patient is more comfortable than by any other method about which we know, and there is a minimum expenditure of effort in nursing care.

However, when third-degree burns are present, it is not ideal. The cleansing and superficial débridement does not remove all the dead tissue. This remains as a nidus for infection and a focus of absorption. These areas must, of necessity, become granulating wounds, with their attendant problems.

Immediate Skin Grafting—In an attempt to fulfil the principles for wound healing *per primam*, we have débrided the third-degree areas, and immediately covered them with split-thickness skin grafts.

Our plan of treatment at present is as follows:

- 1 To be acceptable for immediate débridement and skin grafting, the burn must have occurred not more than six hours previously. With experience it may be possible to extend this time limit.
- 2 Hematocrit and plasma protein determinations are made at once.
- 3 Parenteral plasma is started.

4 Under anesthesia, the burn is washed with soap and soft gauze for ten minutes. This removes the blisters and desquamated epidermis from the second-degree areas. The cleansing is completed with a saline flush. No antiseptic is used.

5 The blood pressure and pulse is carefully watched for any signs of incipient shock, and the plasma administration is governed accordingly.

6 Obvious third-degree areas are completely excised, and hemostasis carefully attended to. If there is doubt about an area being third-degree in depth, it is not excised, as it is in these questionable areas that hair follicles and glandular remnants are usually present in sufficient amounts to allow spontaneous epithelization.

7 Grafts of about 0.010 of an inch thickness are cut with the dermatome and sutured over the excised areas.

8 The donor areas are dressed with one thickness of vaselined gauze smoothly applied, and a snug sterile gauze-roll bandage.

9 The entire burned area is dressed in the same manner. A voluminous gauze dressing is applied over the vaselined gauze and this is held in place under some compression by either Ace-bandage or stockinette applied as a roller-bandage.

10 Adjacent joints are immobilized by the application of plaster encasement directly over the dressing.

11 Plasma, saline or whole blood is administered during the postoperative period as indicated by frequent hematocrit, plasma protein, and Hb determinations.

12 The dressing is not disturbed for 14 days unless a mounting fever or other signs indicate that infection has occurred.

13 If the area is healed on removal of the first dressing, a second dressing of vaselined gauze, a thin layer of dry gauze, and an elastic roller-bandage is applied. This is worn as protection for another 14 days. It is then removed and treatment terminated.

This method of treatment and the postoperative course is illustrated in the following case report.

Case 3—S M H, No 188918, D B white male, age 11, was admitted to Strong Memorial Hospital, one-half hour after being burned on the back. He was not in shock—B P 150/85, pulse 100. He was in considerable pain. The burn as estimated by Berkow's charts, covered about 8 to 10 per cent of the body. It involved the back and a small area over the posterior aspect of the left upper arm. Cold cream had been applied to the burned area.

In the central portion of the burn on the back the skin was an ivory-gray color. About this there was a wide zone of hyperemia on which there were large, weeping areas, intact blebs, and hanging shreds of epidermis. An hematocrit reading, 45 minutes after injury, was 49.3, and the plasma proteins 6.58. He was treated by the method outlined above. During operation, and the immediate postoperative period, he was given 600 cc of whole plasma and 250 cc of saline. No shock occurred. His postoperative course was satisfactory. The temperature never rose above 38.7°C (101.5°F) and returned to normal on the seventh postoperative day. From the fifth postoperative day

IMMEDIATE SKIN GRAFTING IN BURNS

FIG 1a



FIG 1b



FIG 2a

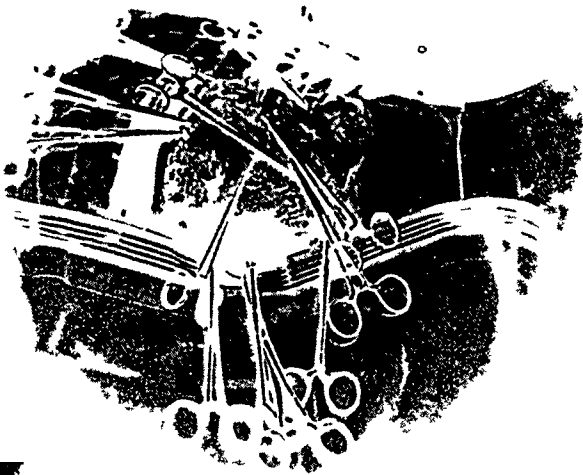


FIG 2b



FIG 3a

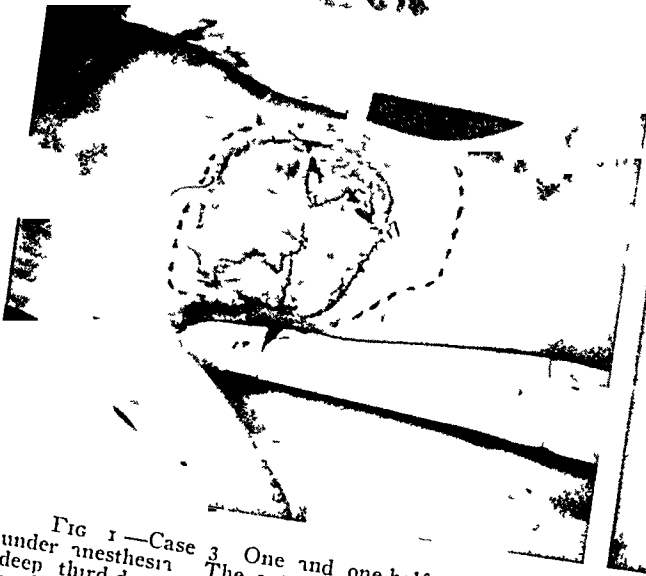


FIG 3b

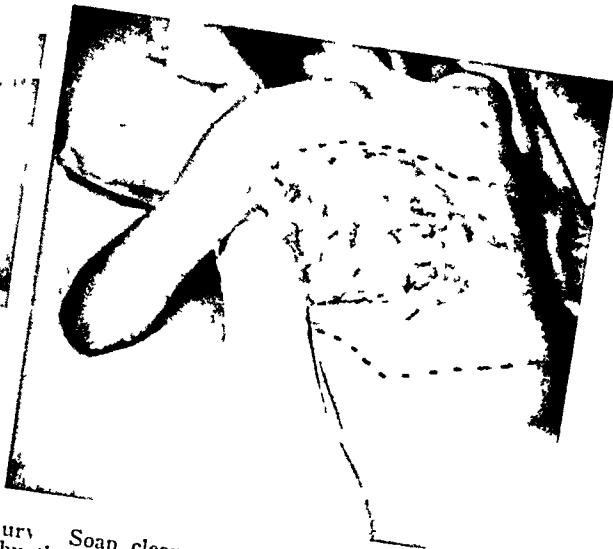


FIG 1—Case 3. One and one half hours after injury under anesthesia. The extent of the burn is indicated by the dotted area. Soap cleansing has just been completed. The white central area is deep third degree burn. Note that cleansing has completely removed all blisters and desquamated epidermis.

FIG 2—Case 3. (a) The third degree area has been completely excised, in places this excision went down to muscle before normal tissue was encountered. (b) Skin grafts, 0.10 inches thick, cut from buttock and thigh and sutured over excised area.

FIG 3—Case 3. Appearance of wound on first change of dressing on the 14th postoperative day. The first and second degree burns have healed and the graft has taken completely. The wound has healed *per primam*. He felt perfectly well and was allowed up. Discharged on 17th postoperative day.

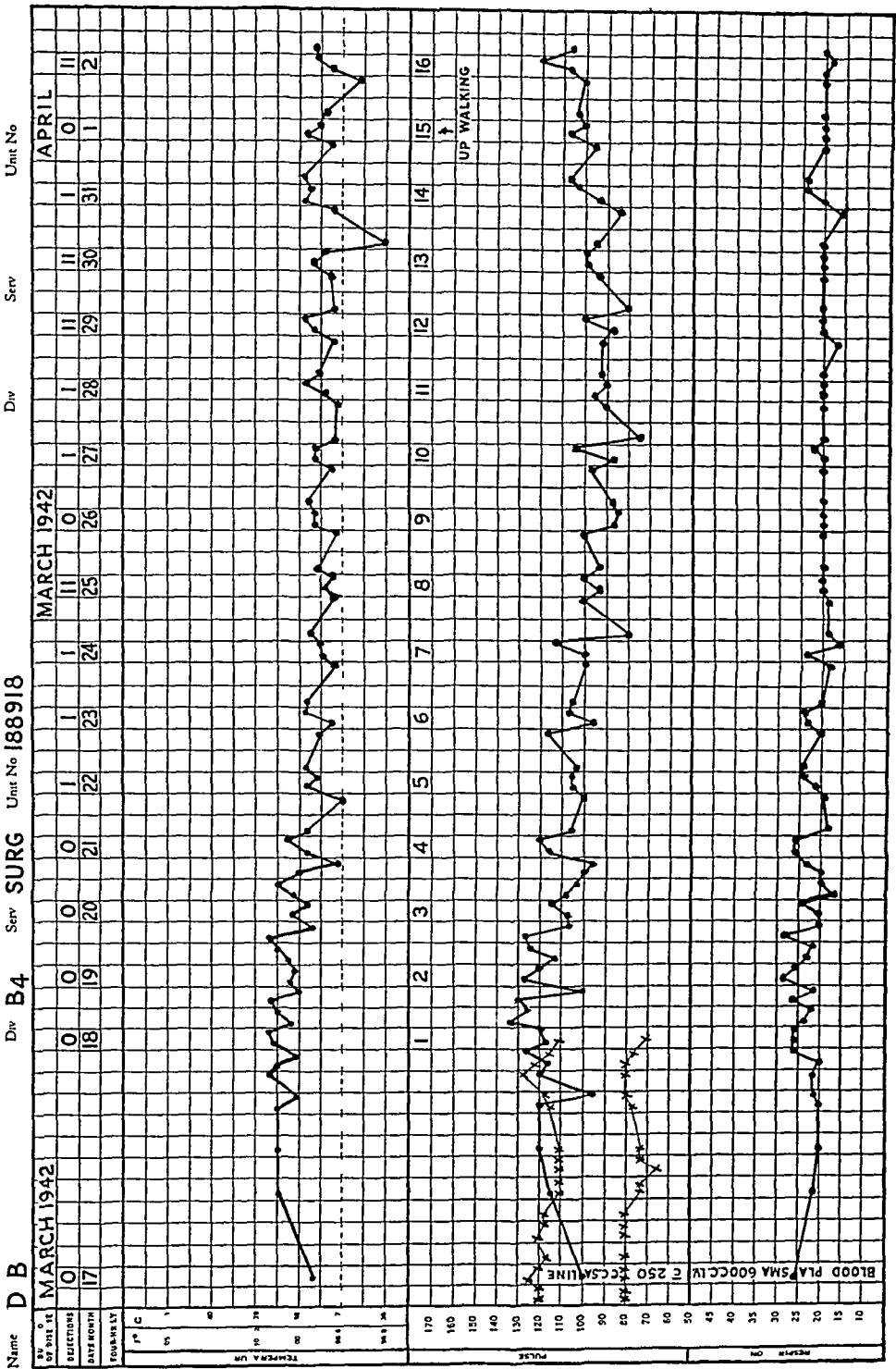


CHART 1 —Case 3 Showing that vital signs returned to normal on fifth postoperative day

on he was comfortable. The dressing was removed on the fourteenth postoperative day. The entire area was epithelized. One small mixed area of third- and deep second-degree burn, which was purposely not debrided, showed the papillary layer, and was sensitive to touch and temperature changes. The remainder of the burn was painless. A new dressing was applied as outlined above. He was allowed up. On the seventeenth postoperative day he was discharged.

TABLE I

TABULATION OF BLOOD STUDIES IN CASE 3 DURING THE INITIAL TREATMENT AND POSTOPERATIVE COURSE
WITHIN 36 HOURS THE VARIOUS DETERMINATIONS WERE WITHIN NORMAL LIMITS

Name	D B		Specific Gravity	Hemato crit	Total Protein	Albumen	Glob	Hb Gm	W B C	Remarks
3-16-42	6 45 P M	1	0272	49 5	6 58	4 15	2 45			45 min after burns, before any treatment
	8 40 P M	1	0266	47 2	6 19	3 84	2 35			After 100 cc whole plasma and cleansing and débridement
	9 30 P M	1	0270	47 1	5 98	3 90	2 08			After 150 cc whole plasma during skin grafting
	11 45 P M	1	0264	44 7	6 16	4 05	2 11			After 300 cc whole plasma and skin grafting
3-17-42	4 00 P M	1	0256	36 8	5 99	3 86	2 13	11 7	10 000	After 600 cc whole plasma plus 250 cc saline i v disc at 4 P M
	9 00 A M	1	0263	33 8	6 20	4 03	2 17			No more i v fluid, taking fluids well p o
3-18-42	11 00 A M	1	0275	43 3						No parenteral therapy
3-19-42								11 8	8 000	
3-20-42	11 15 A M	1	0271	43 2	6 23	3 57	2 76			
3-21-42								11 3	6 500	
3-22-42										
3-23-42								11 5	8,100	
										Total 600 cc plasma (whole) 250 cc saline

CONCLUSIONS

1 Burns are traumatic wounds, accompanied by local loss of blood plasma both from the weeping surface and into the tissues. This plasma loss produces shock by depleting the circulating plasma.

2 Ideal treatment of burns should accomplish the following: Restore lost plasma, prevent further plasma loss, prevent absorption of burned tissue, forestall infection, and promote primary healing.

A first- and second-degree burn, given proper care, will heal *per primam*. A third-degree burn, treated by former methods, can heal only by second intention.

4 By the immediate cleansing and *complete débridement* of a burn, with immediate grafting of deeply injured areas, plus the application of the usual compression dressing and immobilization used over free grafts, it is possible to obtain primary healing of the entire wound.

REFERENCE

- ¹ Mason, Michael L. Local Treatment of the Burned Area. Surg, Gynec & Obst, 72, 250, February, 1941.

THE ELECTRO-ENCEPHALOGRAPHIC DIAGNOSIS OF SUBDURAL HEMORRHAGE

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AND

MARK ALBERT GLASER, M D

LOS ANGELES, CALIF

THE CLINICAL DIAGNOSIS AND LOCALIZATION of subdural and extradural hemorrhage are at times impossible. When such hemorrhage is suspected, it is customary to carry out multiple perforator and bur openings to verify the diagnosis.

The electrical activity of the human cortex, as recorded by the electro-encephalogram, may be modified either temporarily or permanently by such cerebral pathology as tumors, diseases, trauma or chemicals.¹⁻⁹ Experimentally produced lesions also definitely modify the electrical activity. The electro-encephalographic wave produced by destructive lesions has been reported by Dusser de Baigne and McCulloch,¹⁰ the wave caused by cortical pressure, without destruction of the underlying brain, has been described by Glaser and Sjaardema.¹¹ In the experimental production of these pressure lesions a characteristic electro-encephalographic wave pattern was produced in rabbits, which consisted of high *beta* waves superimposed upon *delta* waves. Both clinical extradural and subdural hemorrhage, when there is no damage to the underlying brain, closely simulates the experimentally produced pressure lesions.

In the present communication we wish to present three cases of verified subdural hematoma, in which these characteristic pressure wave patterns were present in each instance, and promptly disappeared after removal of the hematoma. These wave patterns, however, seem not to be pathognomonic of subdural hematoma, or even pressure lesions, because they have been found in hydrocephalus, meningioma, tuberculoma, Parkinson's disease, syphilis, and in a few instances of brain trauma, without operable hemorrhage.

CASE REPORTS

Case 1—R. R., female, age 27, referred by Dr. J. M. Harris, gave a history of a head injury 15 days prior to admission to the hospital. Surgery revealed a right fronto-temporal subdural hematoma. The electro-encephalogram gave the characteristic wave pattern. These waves disappeared 24 hours after operation, and the brain was entirely normal at the end of six months.

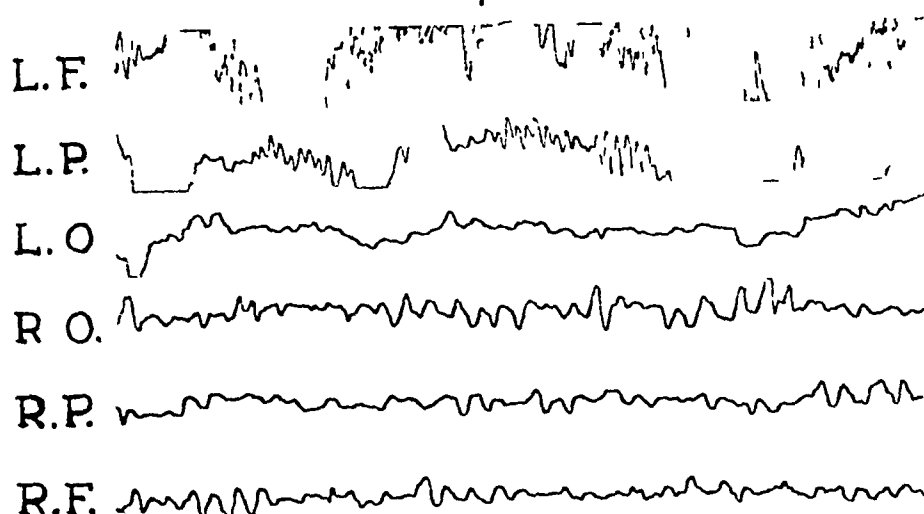
On August 16, 1940, the patient fell, striking her head on a stove. She was unconscious approximately 12 hours. Headaches, that were present for approximately one week, were constant, and situated on the right side. In addition, she had nausea and some vomiting.

Physical Examination—The patient was a well built young woman, weighing 125 pounds, pulse 84, respirations 20, temperature 98.6°F, blood pressure 115/80. Her general physical examination was essentially negative. *Neurologic Examination*—The

SUBDURAL HEMORRHAGE

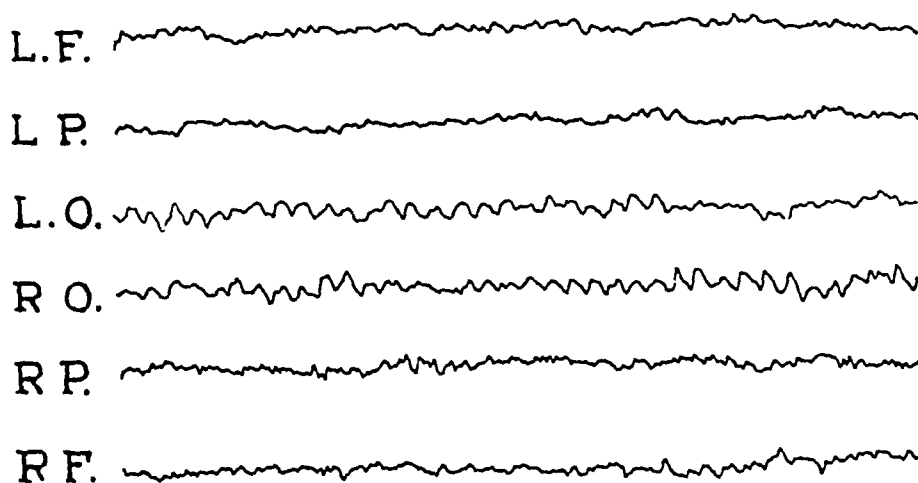
-A-

Pre-operative



-B-

1 Month Post-operative



-C-

6 Months Post-operative

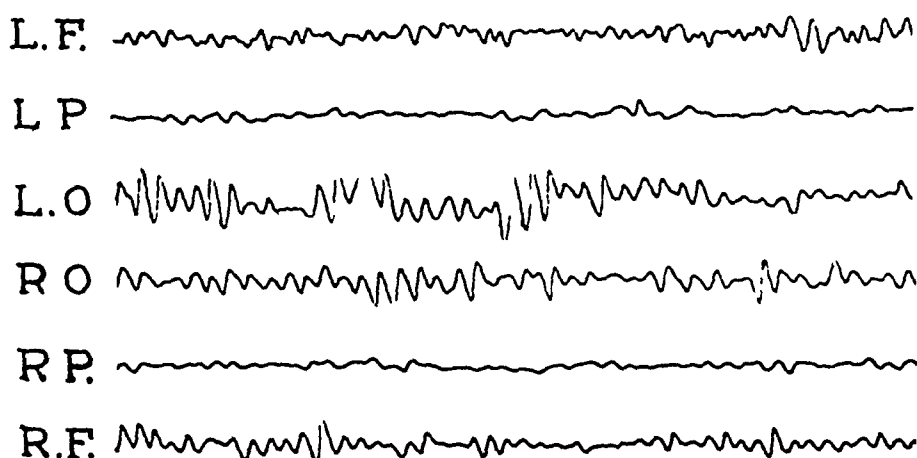


FIG 1—Case R R Right Prefrontal Subdural Hematoma The location of the leads are designated as follows L F—left frontal, L P—left parietal, L O—left occipital, R O—right occipital, R P—right parietal, R F—right frontal

A Note the high voltage beta waves present in addition to the delta waves in R F and R P

B Delta waves are still present in R F

C The electroencephalogram is normal

pupils were very small though not pin-point, reacted normally to light and distance, and had to be dilated to visualize her disks. These showed blurring of the margins. The remaining neurologic examination was entirely normal except that the grip in her right hand was 120 compared to 138 in the left hand, and that her reflexes were moderately active in the arms, but hyperactive in the lower extremities. There were no pathologic reflexes. A spinal puncture, on two occasions, revealed a pressure of 550 mm of water.

The electro-encephalogram revealed a localized area of abnormal electrical activity. This area was located in the right prefrontal region and extended close to the right motor area. The following abnormalities were observed: 1. Slow *delta* waves of approximately one cycle per second and around 100 microvolts. 2. Rapid waves of about 16 to 25 cycles per second, and from 10 to 20 microvolts. These abnormalities were not present in the corresponding areas of the left hemisphere (Fig. 1A).

Operation—On the basis of her right-sided headache, localized in the frontoparietal area, the high intracranial pressure, and the characteristic electro-encephalographic waves, exploration was undertaken. The operation was performed under local anesthesia. A skin incision was made in the frontotemporal region, approximately two inches in length. A perforator and bur opening was made in this area. The opening was enlarged with a rongeur. The dura was extremely vascular and exquisitely tender to touch. Cutting the dura caused considerable local pain. When the dura was grasped with forceps an acute sharp pain was referred to the area of the headache and further radiated toward the ear. Beneath the dura was observed the dark-reddish capsule wall, which was extremely soft to palpation. A thin hypodermic needle was introduced through this capsule and one cubic centimeter of brownish-red fluid was withdrawn. The capsule was then opened and about 50 cc of fluid removed. By careful dissection and washing, this entire structure was removed. The capsule was about ten times as thick as the dura. The underlying brain was compressed by the hematoma in such a way as to leave nearly a half inch space beneath the skull. The cranial opening was approximately in the posterior middle part of this large hematoma, and the capsule extended around this opening in all directions but mostly anteriorly and laterally. The wound was then closed and dressing applied. No drain was inserted. The patient made an uneventful recovery, and was discharged three weeks postoperative.

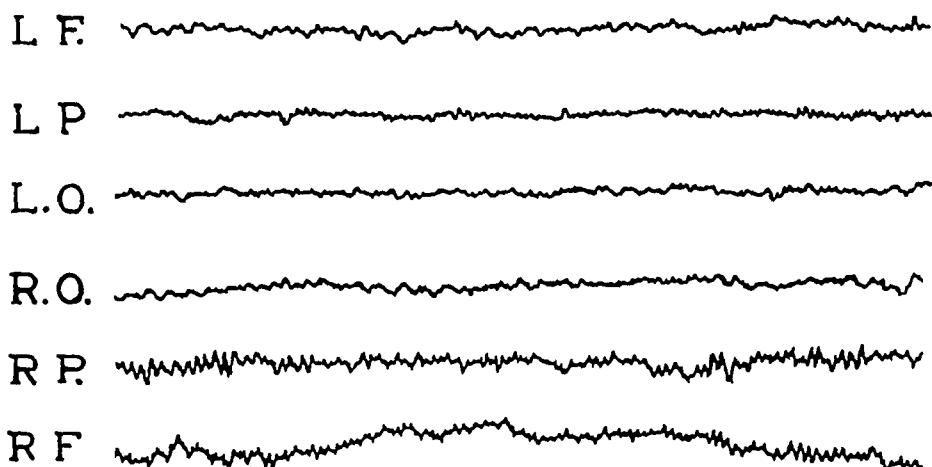
Subsequent Course—The electro-encephalogram taken one month after the removal of the subdural hematoma, in the indicated area, revealed some slow *delta* waves in the right frontal region. The *beta* voltage, however, had returned to normal (Fig. 1B). The electro-encephalogram recorded six months postoperative was entirely normal (Fig. 1C).

Case 2—From the Neurosurgical Service of the Cedars of Lebanon Hospital, March 10, 1940. E. R., male, age 66, had a head injury four months prior to hospital entry. Surgery revealed a left frontoparietal subdural hematoma. Characteristic electro-encephalographic waves were present. The combination waves disappeared 24 hours after operation. Within six months after surgery the *delta* waves disappeared and the electro-encephalogram was entirely normal.

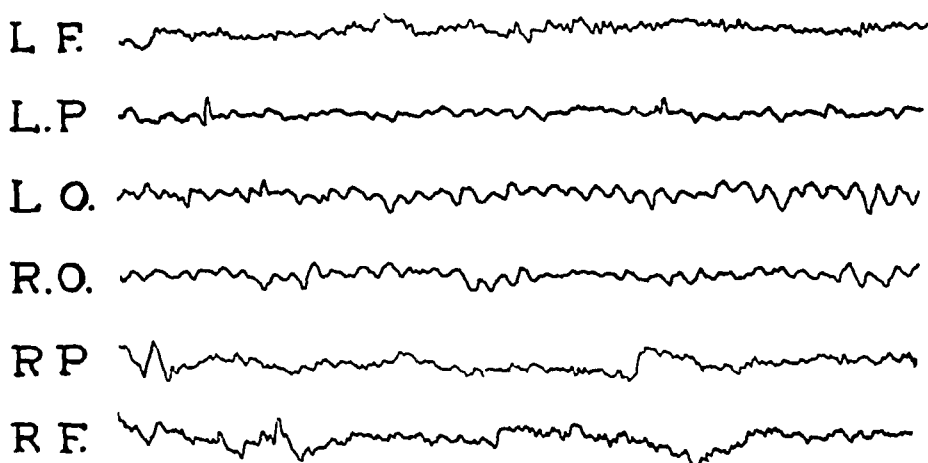
In November, 1939, the patient fell in the bathroom and injured the right side of his head. A large hematoma of the scalp developed. It was not definitely determined whether he had had an unconscious episode and fell or whether he slipped and fell. He remained unconscious for about three minutes and when he recovered the right side of his face was found to be contused and his right thumb pained. He was seen by a physician on 12-19-'39, at which time a drooping of the right side of his mouth was noted, an absence of the right biceps, and of both Achilles reflexes. He also complained of some loss of hearing in the left ear, and weakness of the right grip. The reflexes on the right were more active than those on the left. A spinal fluid examination at this time revealed a total protein of 225 mg per 100 cc. On 2-26-'40 there was some weakness of

SUBDURAL HEMORRHAGE

-A- Pre-operative



-B- 1 Month Post-operative



-C- 6 Months Post-operative

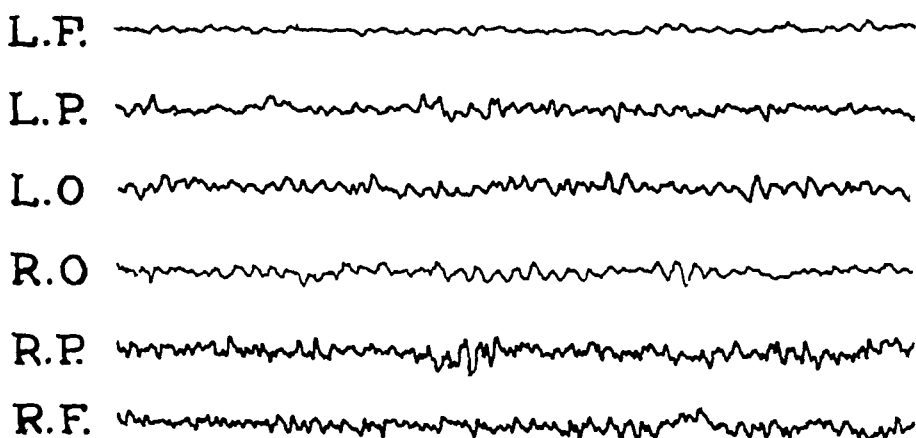


FIG. 2—Case E. R. Left Frontoparietal Subdural Hematoma
A Combined high beta and delta waves in L. F., and L. P. Low deltas in L. O. and R. O.
B Delta waves in L. F. Remaining leads normal
C Electroencephalogram normal

his right leg. About March 1st, the weakness of his right leg increased and he developed attacks of dizziness. He had complained of headache since the time of his fall. On March 7th, he developed weakness, unsteadiness and incontinence of urine, as well as periods of mental confusion. On March 10th, he became stuporous, and was admitted to the Neurosurgical Service of the hospital. He was confined to bed, had Cheyne-Stokes respiration, was irrational, pulse 45, blood pressure 130/90. Physical examination was essentially negative.

Neurologic Examination—There was a definite rigidity of his right arm and leg, associated with weakness. He was irrational but responded at times to questions in a very slow and confused manner. He was unable to write. The reflexes of the arms were subnormal, the abdominal and cremasterics were absent, and the patellar and Achilles reflexes were subnormal. A spinal puncture revealed a pressure of 225 mm of water.

On electro-encephalographic examination both occipital areas showed low *delta* in addition to the regular *alpha* waves. The *alpha* voltage was from 50 to 70 microvolts, and the frequency nine cycles per second. The *deltas* were from 50 to 70 microvolts and the frequency around one cycle per second. In the left motor and frontal areas a combination of *delta* and *beta* waves of increased voltage was observed. In this area the *delta* waves were from 75 to 150 microvolts, and about one cycle per second. The *beta* waves were from 15 to 40 microvolts, and from 16 to 25 cycles per second. The right motor area had a smaller amount of *delta* waves, not higher than 75 microvolts (Fig 2A).

Operation—Under local anesthesia, a subdural hematoma was found in the left frontoparietal region. The hematoma contained approximately 100 cc of fluid. After this was removed the underlying brain became visible, and promptly began to pulsate. The brain, however, did not return to the surface of the skull. The entire dissection of the wall of the hematoma was carried out through the perforator and bur opening. Within a few minutes after the hematoma was removed he became quite rational and was able to write his name. He left the operating room in excellent condition.

Subsequent Course—One month postoperative low *delta* waves were shown in the left frontal area, whereas the other regions showed normal pattern (Fig 2B). Electro-encephalogram taken six months postoperative was entirely normal (Fig 2C).

Case 3—Referred by Dr L. Gaulden and Dr G. Esker. R. O., male, age 66, was injured March 11, 1941. The electro-encephalogram showed combination wave patterns. Operation revealed an acute subdural hemorrhage in the right frontoparietal area. The increased *beta* waves disappeared after operation. The patient expired.

This man fell a distance of 12 feet, striking his head, and was rendered unconscious. He had a pulse of 65, respirations 24, temperature 101°F, blood pressure 120/80. There was severe saggillation over the right eye, his nose bled profusely, and he vomited blood. He had a marked contusion over the right frontal region, pupils were dilated, reacted sluggishly to light, and the right pupil was slightly larger than the left. A slight facial paresis existed. There was no evidence of weakness of the extremities. All the reflexes were absent. Spinal puncture revealed a pressure of 400 mm of water, the fluid was bloody, and showed a count of 60,000 red and 100 white cells per cubic centimeter.

Delta waves, of about one cycle per second and up to 150 microvolts, were present in the right frontal and temporal parietal areas upon electro-encephalographic study. In addition there were high *beta* waves, up to 25 microvolts, and 15 to 25 cycles per second in this area. The left occipital area showed *delta* waves up to 100 microvolts, and around two cycles per second. The *beta* waves were increased in all areas (Fig 3).

In view of the high intracranial pressure, the facial weakness, and the characteristic electric waves over the right frontal region, the diagnosis of subdural hematoma, as well as severe brain damage was made.

Operation—Under novocain anesthesia, an incision was made over the right frontal area, and a perforator and bur opening was made into the skull. The dura was under

tension, somewhat roughened, and vascular. When it was incised a clot oozed out. The skull opening was then enlarged to about the size of a silver dollar. This blood clot extended to the base of the skull, to the edge of the temporal lobe, frontal lobe, and posteriorly as far back as the edge of the ear. It covered the entire hemisphere, and extended to the midline as far as the falx. It was about one and one-half inches thick. By washing, suction, and stripping with cotton and forceps, the entire clot was removed. The original clot must have contained approximately 300 cc of blood. After it had been removed the brain was found to be markedly depressed and the vessels over the cortex dilated. In addition, the dura was extremely vascular. The roughness and vascularity of the dura prolonged the operation considerably because of the continuous oozing of blood. The wound was then closed.

Postoperative Course—A plasma transfusion was administered immediately and a blood transfusion later in the evening. The patient's condition postoperatively was not particularly bad, and his pulse and blood pressure again returned to normal. During the night he did fairly well. About 3:00 A.M. his respirations began to change, and his blood pressure became lower. About 6:00 A.M. his condition was poor and it was quite evident he would not survive. The dressing was then opened and no evidence of bleeding was found, an, however, issued from the wound with each respiration of the patient, indicating that the fracture had extended through the nasal sinuses. A spinal puncture was performed and the pressure found to be 100. The patient expired, 3-11-41, at 1:55 P.M.

Autopsy—Fractures of the upper ribs on the right side, considerable bleeding in the subparietal space, and some bleeding within the thorax was found. When the brain was removed there was no evidence of hemorrhage apparent. At the tip of the frontal lobe could be seen a large laceration which extended to a depth of two inches. The orbital plate was shattered, more on the right than on the left side, with numerous fracture lines running into the ethmoid and sphenoid sinuses, both of these being filled with blood, which accounted for the bloody vomitus that the patient had. Another fracture line chipped off the tip of the sphenoidal ridge. A chip of this bone had entered the cavernous sinus. It was the bleeding from this that infiltrated along the base of the skull and the hemispheres. On top of the orbital plate was an area, the size of a twenty-five-cent piece, which was depressed and spiculated upward into the cranial cavity. Some of this bone had entered the tip of the frontal lobe. Upon removal of these spicules, pieces of brain could be seen adhering to them. In addition, there was a fracture of the right pelvis. The tissues in the posterior peritoneal space were markedly contused and there was a considerable amount of hemorrhage along the ureter, bladder and surrounding tissues.

Gross pathology of the brain revealed a small amount of subarachnoid hemorrhage, with staining of the meninges, most marked in the left parietal region. There was a small contusion in the subfrontal region, which measured 2.5 x 1.5 cm in greatest diameters. There was also a small cortical hemorrhage, 8 mm in diameter, at the tip of the right frontal lobe. Otherwise no gross lesions of the brain were evident. Specific attention was given to the left occipital lobe, where no grossly visible lesion was evident. A block of tissue, however, was taken from this area for microscopic study, and also from the right frontal lobe in the region of the contusion. Section through the brain at the level of the thalamus showed a small bruise of the right hippocampal gyrus as well as the medial cortex of the parietal lobe. The location of these contusions are indicated on the drawings accompanying Figure 3.

Pathologic Diagnoses—Gross 1. Minor subarachnoid hemorrhage, chiefly left parieto-occipital. 2. Right subfrontal contusion. 3. Minor contusion tip of right temporal lobe. 4. Minor contusions of right hippocampal gyrus. 5. Minor contusions of medial aspect of right parietal lobe.

Microscopic—Section through the left occipital lobe shows some slight thickening of the meninges, which is not uniform, and which shows no evidence of focal proliferation. There are no observed architectural alterations. The large nerve cells, however, stain poorly. Some of them show acute alteration in the form of acute degenerative changes and a number of them show fatty degeneration. This degeneration is evidently a chronic process and bears no relationship to any recent change. These chronically altered cells, however, show these acute changes in the form of loss of Nissl's substance and actual degenerative changes in the cell body. Otherwise, no conspicuous alterations were to be found.

Section from the right occipital lobe shows no essential alterations other than the fatty change in the large nerve cells, which in this section seem less profoundly altered as compared with the left side. The Nissl's substance in these cells is partly retained.

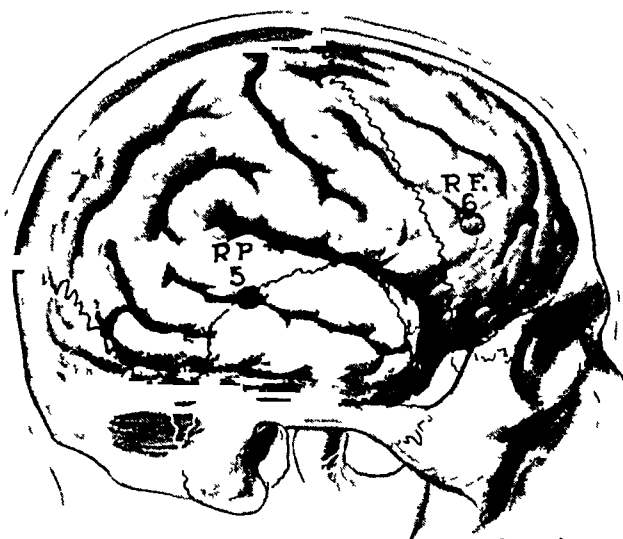
Section taken through the contused area in the right subfrontal region shows a pallor of the affected tissue and in this pale area a few small petechial hemorrhages are found. This contusion involves both the cortex and subcortex over a considerable area and extends fairly deeply into the white matter. *Microscopic Diagnosis* 1 Subfrontal contusion, right. 2 Acute degenerative changes in the nerve cells of the left occipital lobe.

Twenty-four hours postoperative, *delta* waves around 150 microvolts, two to three cycles per second, were found in all areas. The increased *beta* waves had disappeared (Fig. 3B).

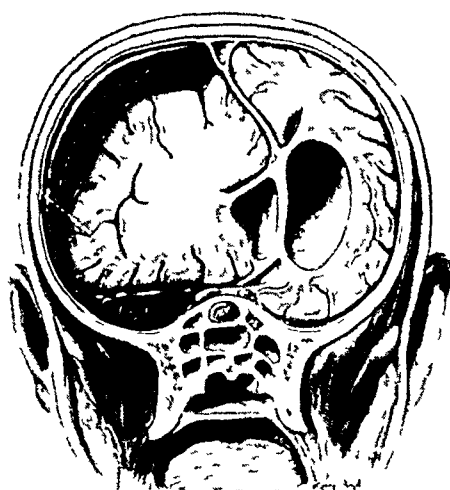
Discussion—In this particular case we not only had a subdural hematoma situated in the right frontal area but we also had a great amount of brain damage as evidenced by the *delta* waves in the other regions of the brain. In spite of the relief of the subdural hematoma by surgery, and its removal, the brain damage was of such severity that the patient expired. We, however, continued recording the waves during the patient's life. These waves continued about 40 seconds after respirations had ceased and the heart action was not audible. The electro-encephalographic recording at this time demonstrated random *delta* waves, and waves of six cycles per second in all areas. The voltage of these waves gradually decreased until the galvanometer did not show any deflexion (Fig. 3C). The patient expired at this time.

In these three clinical cases in which a subdural hematoma was verified by operation, a combination wave pattern was found. In all of the cases, it disappeared after surgical removal of the lesion. This wave pattern consisted of 1 *Delta* waves of around one to two cycle waves per second, and 100 microvolts, and up 2 *Beta* waves alternating or superimposed upon the *deltas* from 16 to 25 cycles per second, and from 10 to 20 microvolts, and up. Although we do not believe this combination pattern is pathognomonic of subdural hematoma, it is noteworthy that we have observed it in cases of hemorrhage wherein a pressure has been applied to the cortex. Taking into consideration the clinical signs and the association of the combination waves, aids in verifying the existence and localization of the hemorrhage.

In over 150 cases of head injury in which brain damage was present, and repeated recordings were taken on the same patient, we have found the existence of these combination patterns in only two instances. In none of the entire series was massive hemorrhage suspected. In the two cases mentioned, repeated electro-encephalographic studies showed a disappearance of



Location of Leads

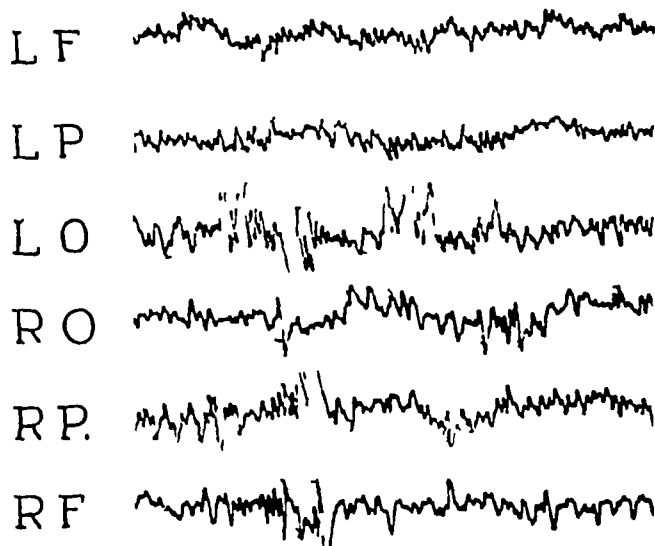


Subdural Hematoma (Schematic)

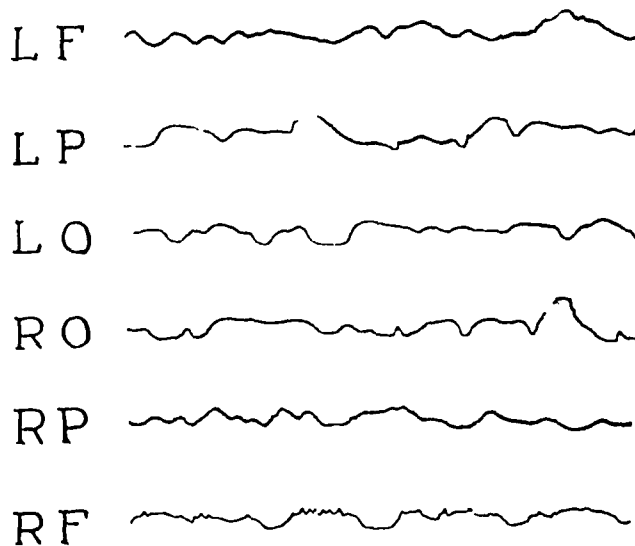


Depressed Fracture of Base
involving Cavernous Sinus

-A-
Pre-operative



-B-
24 Hours
Post-operative



-C-
Waves Prior to Death

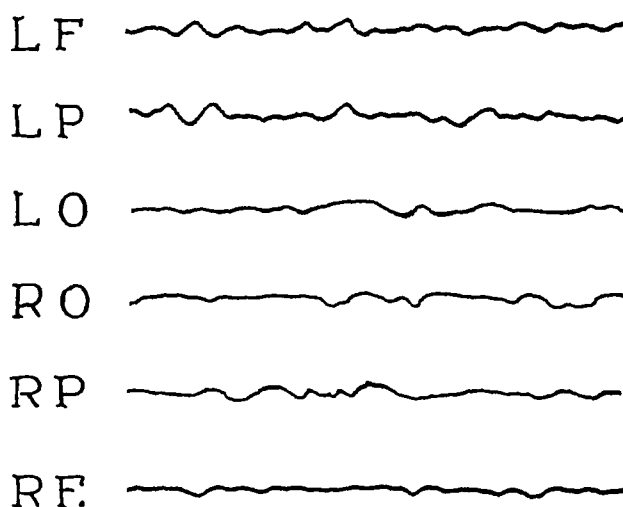


FIG 3—Case R O Right Frontoparietal Subdural Hematoma
A Combination of high betas and deltas in R F and R P
B Delta waves in all areas Increased beta has disappeared
C Diminution of electrical activity in all leads

the combination patterns, and at no time did we have sufficient clinical data to arrive at a diagnosis of large subdural hemorrhage

CONCLUSIONS

1 In three verified cases of subdural hematoma an electro-encephalographic wave pattern consisting of high voltage *beta* combined with *delta* waves was found, which disappeared when the hemorrhage was removed

2 This wave pattern is not pathognomonic of subdural hematoma but has been observed in hydrocephalus, meningioma, syphilis, Parkinson's disease, tuberculoma, gumma, and head injuries

3 The pattern is of value as an adjunct in confirming the diagnosis of subdural or extradural hematoma when the clinical signs and symptoms have indicated such condition to be present

REFERENCES

- ¹ Williams, D., and Gibbs, F. A. Localization of Cerebral Lesions by Electro-encephalography. *Tr Am Neurol Assn*, **64**, 130-134, 1938
- ² Walter, W. G. Electro-encephalography Aid to Diagnosis. *Bristol Med-Chir J*, **57**, 1-8, 1940
- ³ Case, T. J., and Bucy, P. C. Localization of Cerebral Lesions by Electro-encephalography. *J Neurophysiol*, **1**, 245-261, 1938
- ⁴ Gibbs, F. A. Interpretation of the Electro-encephalogram. *J Psychol*, **4**, 365-382, 1937
- ⁵ Gibbs, F. A., Davis, H., and Lennox, W. G. The Electro-encephalogram in Epilepsy and in Conditions of Impaired Consciousness. *Arch Neurol & Psychiat*, **34**, 1133-1148, 1935
- ⁶ Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. Epilepsy. Paroxysmal Cerebral Dysrhythmia. *Brain*, **60**, 377-388, 1937
- ⁷ Hoagland, H. On the Mechanism of the "Berger Rhythm" in Normal Man and in General Paretics. *Am J Physiol*, **116**, 77-78, 1936
- ⁸ Jasper, H. H., Kershman, J., and Elvidge, A. Electro-encephalographic Studies of Injury to the Head. *Arch Neurol & Psychiat*, **44**, 328-348, 1940
- ⁹ Glaser, M. A., and Sjaardema, H. The Value of the Electro-encephalogram in Craniocerebral Injuries. *Western Jour of Surg, Obst and Gynec*, **48**, 689-696, 1940
- ¹⁰ Dusser de Barenne, J. G., and McCulloch, W. S. Some Effects of Laminar Thermo-coagulation upon the Local Action Potentials of the Cerebral Cortex of the Monkey. *Am J Physiol*, **114**, 692-694, 1936
- ¹¹ Glaser, Mark Albert, and Sjaardema, Hendrickus. Electro-encephalographic Diagnosis of Extradural and Subdural Hemorrhage. *Proc Soc Exper Biol & Med*, **47**, 138-140, 1941

THE USE OF MYOTOMY IN THE REPAIR OF DIVIDED FLEXOR TENDONS

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DESPITE some notable contributions, the literature of tendon surgery remains persistently optimistic and narrowly technical. While it is the purpose of this report to present still another operative innovation, an attempt will be made to consider its application from the larger viewpoint of hand function.

This can, perhaps, be best done by outlining a general attitude toward the subject of repair of the divided flexor tendon. Let us discard our ambiguous notions of percentages of good or bad results in favor of an analysis of the individual case in terms of controllable and uncontrollable factors.

Among the latter we must list these: The physical nature of the wound, its location in the hand, the degree and nature of contamination, the amount of bruising of the tissues, the extent of stripping of the tendon sheath, and the time-interval before treatment and the presence of complicating fractures. These are the readily recognizable elements that go far to determine an end-result before an instrument has been introduced into the wound.

In addition, there are two other less apparent characteristics of each case that may weigh quite heavily in the final balance. The first is the construction of the injured hand. Does it resemble the pulpy, calloused hand of the laborer, or the dextrous, trim fingers of the artist? The second is the personality of the patient. Is he cooperative and assiduously helping along the restoration of his hand to normal, or does he assume a negativistic attitude and sullenly refuse to move the affected fingers between treatments? There is literally a physical and mental diathesis in each patient which has much to do with the outcome. A willing patient cannot spontaneously dissolve a gallstone or absorb a chest full of pus, but he can work wonders over a period of months with a stiff finger whose flexor tendons may have seemed to be sheathed in very dense adhesions.

While certain technical expedients may serve to ameliorate the untoward effect of any of these uncontrollable factors, they remain as major determinants in the fate of any case regardless of the details of treatment.

The controllable factors are those that become manifest after the patient entered the hospital. They are: The decision for immediate or delayed tenorrhaphy, the use of a tourniquet, the employment of a proper technic as regards exposure, suture material, and handling of the tissues, and the assignment of one interested member of the staff to the care of every case from reception to final discharge. The importance of each of these

has been repeatedly emphasized by Koch and Mason,¹ Bunnell,² and Mayer,³ so that any further discussion here would indeed be superfluous.

In short, this method of analysis demonstrates the futility of applying the statistical method to a series of tendon cases. Even if the number were extremely large, the many variations of uncontrollable factors alone would render impossible the selection of similar samples in the evaluation of any proposed method or technical maneuver. Furthermore, between the excellent result of complete return of function and the extreme typified by the useless flopping finger are intermediate grades of recovery to which the ambiguous terms good, fair, indifferent and poor are variously applied.

To make matters more complicated the fingers are not of equal functional importance since they decrease in usefulness from the index to the fifth fingers. Also, the essential joint of the thumb is the metacarpophalangeal while that of the other fingers is the proximal interphalangeal joint, a fact of the greatest importance which is commonly overlooked. It is possible to have a satisfactory finger with poorly functioning terminal phalangeal and metacarpophalangeal joints as long as the proximal interphalangeal joint is normal. However, if the motion of the latter is impaired as a sequela of tendon injury, the finger is proportionately crippled.

Thus, the nature of this subject is such that it is as difficult to appraise one's own results as it is to criticize those of others. It is for this basic reason that the method of clinical exposition has been chosen to present the procedure of myotomy as an auxiliary to tendon repair.

Myotomy is designed to control an hitherto uncontrollable factor, *i. e.* muscle tension on the divided tendon. This exerts its influence from the moment of injury throughout the period of convalescence. At the time of the trauma, it causes the characteristic separation of the tendon ends. There is varying difficulty as the proximal end is found, seized and brought down into the wound for suture. During the first month of convalescence this muscle tension tends to disrupt the site of repair by its continuous dehiscence effect. It is only after the first three to four weeks, when the tendon is sufficiently healed, that this adverse effect is transformed into a beneficial one, pulling on the tendon in the sheath and so tending to elongate and resolve the adhesions.

Ordinarily, the only means taken to minimize muscle tension is the application of a moulded plaster splint immediately after tenorrhaphy with the wrist and fingers in acute flexion. While this rests the muscle and does decrease its tension, it far from obviates the pull at the suture site. This fact is amply demonstrated by the very real tension invariably found as divided flexor tendon ends are being brought together with the patient under complete anesthesia. Despite the immobilizing splint normal muscle tone exerts its continuous dehiscence force on the suture line during the post-operative period. It is this hitherto uncontrollable factor which has made hazardous the immediate institution of active motion after repair. In fact

it was just such an unfortunate accident the rupture of a tendon repaired six days before, that served as the stimulus for this work

Aside from the original report,⁴ there are only two relevant articles. The first by Moser,⁵ in 1927, is a short statement to the effect that the retraction of the proximal portion of the divided tendon can be prevented by infiltration of the muscle bellies in the forearm with novocain solution. There are no case reports. The other communication, by McNealy and Lichtenstein,⁶ in 1931 is an experimental study, in dogs of the stages of retraction in a muscle after its tendon has been divided and of the beneficial effect of interrupting the nerve supply.

The rationale of myotomy is quite simply, the mechanical interruption of the continuity of the tendon with the major portion of the muscle fibers inserting into it. This leaves only those few muscle fibers functioning that are distal to the point of selection and, therefore, still in continuity with the tendon. This obtains until such time as the myotomy wound has healed and the contractile force of the muscle fibers proximal to the site of myotomy is again transmitted to the tendon.

The flexor muscles of the forearm are of the unipennate and bipennate types with the tendon prolonged throughout the length of the muscle. The muscle fascicles are short and stem from their bony and fascial origins to insert obliquely into the corresponding tendon prolongation which courses along the volar aspect of the muscle to become the tendon in the carpal tunnel and hand. It follows that division of the tendon prolongation results in a loss of contractile power, the degree of which is related to the location of the point of interruption.

The origins of these flexor muscle fibers extend more distally than is shown in the anatomic atlases, so that because of the obliquity of these fascicles, the more distal extend into the carpal tunnel as they unite with the tendon. In fact, the tendons of the flexor digiti quinti are commonly enveloped in muscle tissue as they enter the carpal canal. For this reason, myotomy can be performed just above the wrist and the amount of muscle tissue to be permitted to function is easily measured as it lies exposed in the wound. With each succeeding case, this point of division has progressed distally as confidence in the spontaneous and complete healing of the myotomy wound with full return of muscle strength has grown. In the first case, myotomy was undertaken at about the junction of the distal third with the proximal two-thirds of a flexor muscle belly. In the last cases, only one inch of muscle fibers remained distal to the selected point of division of the tendon prolongation.

The procedure is quite simple and performed in a few minutes. After the divided tendon ends in the hand wound are identified a short linear incision is made just above the wrist with clean gloves and instruments. The fascia is divided and then, with an artery forceps, the paratenon tissue is gently separated until the corresponding muscle is identified. This is

rendered easy by gently tugging on the proximal tendon end in the hand wound. The forceps is then passed deep to the muscle delivering it into the wound as shown in the illustration. The point of division of the tendon prolongation is then selected, leaving about one inch of muscle fibers to

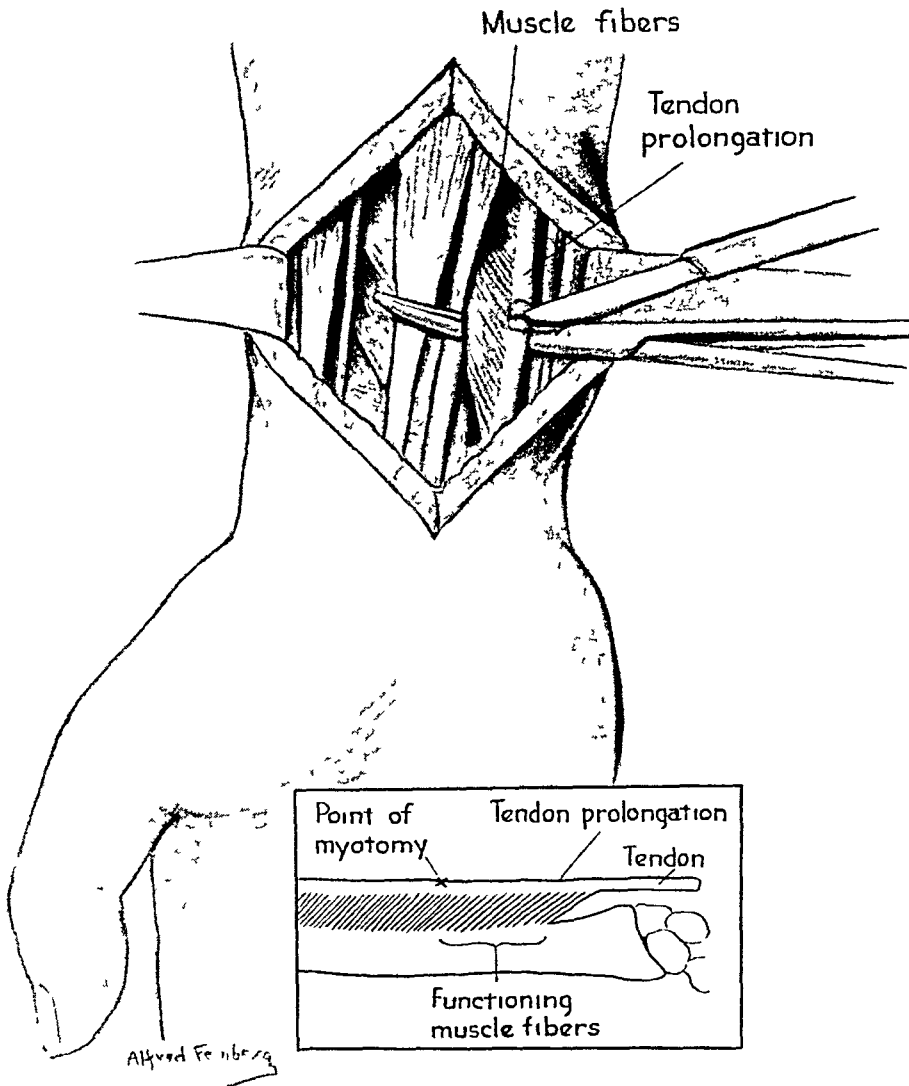


FIG 1—The method of dividing tendon prolongation by delivering the muscle into wound after dissecting it free from the enveloping paratenon. Note the distribution of the muscle fibers, particularly as shown in the inset, which is a schematic lateral view at the same level.

function below it. This is labeled “functioning muscle fibers” in the illustration.

As the tendon prolongation is cut, two things can be noticed. The first is the marked diminution of the tension with which the cut tendon ends in the hand can be approximated. The second is the actual transposition of the tendon distally into the hand as the myotomy wound gapes, usually one-half to three-quarters of an inch. The fascia and skin are then closed, and the procedure returns to the hand.

On an empiric basis of a dozen unselected cases, myotomy as an auxiliary to flexor tenorrhaphy possesses the following characteristics

- 1 It is an easily performed, short procedure
- 2 It facilitates the handling of the divided tendon ends by eliminating the tension which ordinarily complicates the repair
- 3 The danger of disruption of the suture line is obviated. This allows early active motion if so desired
- 4 Much finer suture material can be used in the tenorrhaphy. In the last cases, arterial silk was employed
- 5 Because of the ease of approximation of the tendon ends, these can be more completely debrided and trimmed without fear of sacrificing too much tendon
- 6 Because of the absence of tension, the finger can be splinted, post-operatively, in extension with only the wrist flexed. This has two advantages. In the first place, it is far easier to regain function in a finger so maintained than in one coiled up in the most acute flexion for three to four weeks. Secondly, in the extended finger the site of tendon suture is withdrawn into the uninjured tendon sheath away from the point at which the sheath, surrounding tissues, and skin were lacerated. These tendons are almost invariably divided when the fingers are in the grasping or acutely flexed position. Thus, the post-operative extension makes for less likelihood of adhesions between the tendon suture site and that of the injury to the sheath and skin
- 7 In secondary cases with marked retraction or loss of tendon substances, myotomy renders unnecessary the use of tendon grafts to bridge short intervals. This is demonstrated in the second and tenth case reports below
- 8 There has been uniform return of muscle strength in all the cases. As would be expected in so richly vascular a tissue, the myotomy wound evidently heals completely and so allows full restoration of muscle function. This was measured in the first case

CASE REPORTS

Case 1—Beekman Hospital No 33783 J P, age 43, was admitted, April 18, 1939, shortly after a porcelain faucet handle crumbled in his right hand. He had suffered a short laceration of the palm of the right hand and, on examination, exhibited complete loss of flexion of the interphalangeal joints of the index finger. There was also anesthesia of the radial half of the palm and of the apposing surfaces of the index and middle fingers. Since the criteria for immediate repair were satisfied, operation was immediately performed. The sublimis and profundus tendons to the right index finger were found to be completely divided. With slight extension of the wound it was possible to seize the divided profundus tendon ends. They were approximated under considerable tension. For this reason, with clean gloves and instruments, an incision was made in the lower third of the forearm through which the corresponding profundus muscle belly was identified and isolated. In the lower third of the muscle a short transverse incision was made through the tendon prolongation, resulting in almost complete relief of the tension at the site of injury so that the divided tendon ends, after the clamps holding

them were cut away, were easily approximated with fine Pagenstecher linen thread using the Connell technic. The hand and finger were placed in about ten degrees flexion and a dorsal plaster splint was maintained for 25 days. During this time, guided active motion was allowed each day except on the tenth, when due apparently to edema, no motion was possible. The wounds remained clean. From the fourth week on radiant heat, massage, and active motion were instituted. The patient returned to work at the end of the fifth week. By the end of the seventh week, there was a normal range of flexion and extension at the interphalangeal joints, with slight restriction at the metacarpophalangeal joints. By the end of the eighth week, he could touch the tip of the finger to the palm. By the twelfth week, the finger could be actively coiled up and moved in all directions with agility equal to that of the normal side. The patient was discharged with a normally functioning finger in the fifteenth week.

Return of muscle power was tested by holding the forearm and finger rigid against a wooden splint and flexing the distal interphalangeal joint over the edge of the splint. At the end of the sixth week, a four-pound weight could be easily moved over a pulley by the terminal phalanx throughout the full arc of flexion. By the twelfth week, an eight-pound weight was easily so moved, by the fourteenth week, nine pounds. Control for the terminal phalanx of the normal index finger was eleven pounds flexion.

Case 2—Beekman Hospital No 36924 E S, age 51, was admitted, December 11, 1940, 23 days after a porcelain faucet handle had crumbled in his right hand, resulting in a wound of the palm which was sutured by a local physician. He came to the clinic for after-care, and it was noticed that there was loss of flexion of the interphalangeal joints of the right index finger and right thumb as well as a loss of sensation along the lateral surface of the index finger and of the web space between it and the thumb. At operation, exposure was obtained by incision along the thenar flexion crease. With considerable difficulty the divided flexor tendon ends of the index finger were dissected free of the scar tissue. The distal end of the flexor pollicis tendon was identified, but it was evident that the proximal end of this flexor pollicis tendon had retracted within the carpal canal where it was coiled back on itself and closely adherent to the other tendons. An incision was made above the wrist for myotomy as well as to assist in the freeing of this proximal portion of the flexor pollicis. However, it was impossible to dissect it free from above either. Since the alternatives of dividing the transverse carpal ligament or of exerting more force and so traumatizing the other tendons and their sheaths were out of the question, the following procedure was performed. The proximal portion of the index sublimis tendon was sutured to the distal end of the index profundus tendon. The proximal end of the index profundus tendon was then swung over to be sutured to the distal end of the flexor pollicis. Because of the tension and the presence of a gap of at least half an inch, myotomy was done on the index profundus tendon. This made possible the suture as described above. Arterial silk was used to unite the tendons and to restore the sheaths as much as possible. Sensory nerve ends in the scar were dissected out and sutured. The wrist was then put up in marked flexion with the fingers extended in the natural position with the aid of a posterior plaster splint. Because a staphylococcus was cultured from the wound at the site of the old blood clot, active motion was not allowed until the end of the third week, the splint being maintained for a month. Physiotherapy was then begun and the patient returned to work involving active use of the hand at seven weeks. Improvement continued progressively until the ninth month. There was normal function of the index finger and only slight restriction of motion of the thumb. The strength of the fingers have practically returned to normal.

Case 3—Beekman Hospital No 36324 C F, age 44, was admitted, August 21, 1940, ten minutes after having caught his right hand in a power saw. He suffered a laceration of the volar aspect of the proximal phalanx of the middle finger with the division of one slip of insertion of the sublimis tendon and a complete division of the profundus tendon and also of the digital nerves. There were other injuries which healed

uneventfully and will not be again mentioned. They were. An avulsion of the nail of the thumb with amputation of the tip, and a laceration of the index finger with partial division of the sublimis tendon. Because of the recent and clean nature of the wound, immediate operation was performed. After identification of the cut tendon ends, myotomy was performed above the wrist and the cut tendon was then sutured with four fine silk stitches, two of the Bunnell type, the tendon ends, of course, being trimmed. A dorsal plaster splint was then applied with the wrist and fingers in 10° to 20° flexion. On the eighth day, guided active motion was interrupted because of the appearance of a stitch abscess which was open. The finger was kept quiet for five days, following which, in view of the rapid healing of the wound, motion was again begun. Physiotherapy was started in the fourth week and the patient went back to work in the sixth week.

Improvement continued progressively until, at the sixth month, there was only slight restriction in flexion of the interphalangeal joints, which was sufficiently small to offer the promise of complete function in the future.

Case 4—Beekman Hospital No 38380 W S, age 42, was admitted, August 18, 1941, six days after both flexor tendons of the right middle finger had been divided by a scissors. The divided tendon ends of the flexor profundus were found through a flap incision over the proximal phalanx. Myotomy was then performed above the wrist and the tendon ends of the finger were then easily approximated with arterial silk. A post-operative plaster splint was applied, with the wrist in flexion and the finger extended. Active motion was allowed throughout the postoperative period. On the sixteenth day, there was some inflammation of the finger wound, and on the twentieth day, pus was released from under the skin flap and a drain inserted. A low grade subcutaneous infection with intermittent discharge of silk sutures continued for nine weeks. At the end of five months, there was about 90° motion in the proximal interphalangeal joint but practically none in the distal joint. This case has obviously formed adhesions due to the infection and will require plastic procedure some time in the future.

Case 5—Beekman Hospital No 38474 H F, age 20, was admitted, August 20, 1941, shortly after dividing the flexor digiti quinti profundus tendon in the middle phalanx of the finger on a sharp piece of metal. There was also a division of the ulnar digital nerve of the finger. Because the wound was dirty, simple skin suture was performed. The patient was discharged. On September 4th, he was readmitted for tenorrhaphy and neurolysis. An incision was made along the radial side of the middle phalanx, and then across the distal flexion crease. This flap was then dissected free, revealing an extensive disruption of the sheath, with several foreign particles present. The tendon ends were dissected free. The procedure of myotomy through the usual incision in the wrist was then performed with marked release of tension. The divided tendon ends were then easily sutured together. The digital nerve was then dissected free and its ends placed together. Because of the contamination a molded plaster splint was kept on for three weeks postoperatively. The patient resumed work in six weeks and at the end of five months, showed a normal range of motion of the distal interphalangeal joint and of the finger. The only residuum was a nontender scar. Sensation returned.

Case 6—Beekman Hospital No 38514 P S, age 28, was admitted, September 11, 1941, shortly after catching his left thumb in the blade of an automatic saw. The wound extended through the digital nerves, the flexor pollicis tendon, and actually grooved the bone. Because of the minimal contamination, immediate tenorrhaphy was performed. There was considerable retraction of the divided tendon ends, as is characteristic of the thumb, and it was necessary to enlarge the opening in the sheath. Myotomy was performed, and it was then possible to approximate the tendon ends with arterial silk. Neurolysis was performed. A molded plaster splint was applied postoperatively and maintained for four weeks, with the wrist in flexion and the thumb in extension. Active motion was permitted at each dressing. Because of the contused nature of the skin wound, and because of an inflammatory reaction with sloughing of the tendon suture, physiotherapy was not begun until the end of the tenth week. Improvement has

been slow, so that while there was full strength of the thumb at the end of five months, there was only about 40° of active flexion in the interphalangeal joint. The patient began working after two months.

Case 7—B. D., age 24, was operated upon by Dr. Myron Sallick, of New York City, January 1, 1941. On that day he had cut his right thumb with a razor blade and had been unable to flex it since. For proper exposure, the tendon ends were identified, and myotomy was then performed above the wrist. The divided tendon ends were then approximated with fine silk sutures. A posterior plaster splint was applied with the wrist in flexion but with the thumb not otherwise immobilized. Convalescence was uneventful and at follow-up three months later, there was a complete return of function and the muscle strength was equal to that of the normal thumb.

Case 8—J. L., age five, was operated upon, June 27th, by Dr. Myron Sallick, because of a divided flexor tendon of the right thumb. The accident occurred two hours before admission and was due to a broken milk bottle. The wound was debrided and the tendon sheath was found to be widely lacerated. The capsule of the metacarpophalangeal joint was opened. On approximating the tendon ends, marked tension resulted. Myotomy was then performed above the wrist with marked relief of the tension. The tendon ends were then resutured with fine silk. Five grams of sulfanilamide were placed in the wound. A posterior plaster splint was then applied with the wrist in semi-flexion, the thumb being left in a neutral position. Despite a gross infection of the wound with a discharge of pus and early removal of the sutures, active motion was present at the end of the third week. The patient was then discharged to the Out-Patient Department, but failed to return.

Case 9—Beekman Hospital No. 36013. B. F., age 30, suffered a division of the left flexor pollicis longus tendon when cut by a broken glass jar. The digital nerves were also divided. After the tendon ends were isolated, myotomy was performed and tenorrhaphy with arterial silk was then easily done. The patient did well, but a secondary contracture due to scar tissue developed. This was not surprising in view of the jagged, contused nature of the original laceration, and the involvement of all the deep tissues, including the capsule of the metacarpophalangeal joint. A secondary plastic procedure was carried out to relieve the contracture. The result was unsatisfactory, since the movement of the thumb is somewhat restricted, despite the fact that the tendon is well healed and causes flexion with normal strength.

Case 10—Beekman Hospital No. 34090. P. C., age 44, was admitted June 13, 1939, shortly after a water bottle crumbled in his left hand. He suffered jagged lacerations of the ring and little fingers. There was no loss of sensation but there was complete loss of flexion of the interphalangeal joints of the little finger. At operation, only the divided profundus tendon ends were seized and brought together at the middle phalanx. As is characteristic of this finger, there was a good deal of tension. For this reason, an incision was made in the forearm just lateral to the ulnar vessels and nerves. The flexor profundus digiti quinti muscle belly was readily identified. About half of the thickness of the muscle was divided resulting in a definite diminution of tension with much easier approximation of the tendon ends. The myotomy wound gaped more than half an inch. The tendon ends were repaired with a fine linen Connell suture. A posterior molded plaster splint was applied with the hand and finger in slight flexion. This was maintained for four weeks. During the second and third weeks there was a loss of the undercut skin overlying the suture site. The mucopurulent discharge from this point was evidently due to sloughing skin and not to a real infection. During the fifth week, there were few degrees of flexion of the terminal phalanx and about ten degrees of the proximal interphalangeal joints. Improvement was slow but progressive, so that at the end of ten months, the range of motion at the proximal interphalangeal joint was about two-thirds normal, and at the distal joint, about one-third normal. The result in this case was adversely affected by the loss of the skin flap due to the nature of the trauma.

Case 11—H R, age 15 months, was admitted to the care of Dr Lester Breidenbach, of New York City, because of a history of inability to flex the left, index, and middle fingers, following a deep laceration of the hand, occurring two months before. Exploratory operation revealed a division of the flexor tendons of the affected fingers. After a most difficult dissection, the ends were identified. Myotomy was then performed above the wrist with a gratifying result, so that the tendons in the hand were fairly easily approximated. Postoperatively, a molded plaster splint was maintained for three weeks. Follow-up at four months, showed an excellent result.

CONCLUSIONS

The adverse effects of muscle tension acting upon the site of tendon repair can be obviated by simultaneous division of the corresponding tendon prolongation in the distal forearm.

The procedure of myotomy is easily and quickly performed, and expedites repair of the divided tendon.

The myotomy wound heals spontaneously and completely, with no residual defect of muscle strength.

REFERENCES

- ¹ Koch, S L, and Mason, N I. Division of the Nerves and Tendons of the Hand. *Surg, Gynec, and Obstet*, **56**, 1, January, 1933.
- ² Bunnell, S. Reconstructive Surgery of the Hand. *Surg, Gynec, and Obstet*, **39**, 259, September, 1924.
- ³ Mayer, L. The Physiological Method of Tendon Transplantation. *Surg, Gynec, and Obstet*, **33**, 528, November, 1921.
- ⁴ Blum, L. Partial Myotomy in Treatment of Divided Flexor Tendons of Hand. *ANNALS OF SURGERY*, **113**, 460-463, March, 1941.
- ⁵ Moser, E. Zur Sehnennaht. *Zentralbl, f, Chir*, **54**, 1606, June 25, 1927.
- ⁶ McNealy, R W, and Lichtenstein, M E. Muscular Relaxation Produced by Novocain as Aid in Tendon Repair. *Surg, Gynec, and Obstet*, **53**, 40-45 July, 1931.

BRIEF COMMUNICATIONS

ARTERIOVENOUS FISTULA

CASE REPORT

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AND

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FROM THE CAYLOR NICKEL CLINIC BLUFFTON INDIANA

WE ARE REPORTING a case of traumatic popliteal arteriovenous fistula which occurred in a man, age 20 This lesion was successfully treated by quadruple ligation¹

When an arteriovenous fistula involves vessels of considerable size the derangement of cardiac function slowly and progressively increases As Pemberton² observed, the larger the leak the greater the volume of blood that will be shunted and the more serious the consequences To maintain adequate circulation to the capillaries nature compensates by increasing the systolic pressure and, also, by increasing the total blood volume³ Although the heart may carry on for many years under the added load caused by a small arteriovenous fistula the circulatory function becomes progressively more upset Because of the increased blood flow the artery proximal to the fistula becomes enormously dilated, this, in turn, causes further enlargement of the fistulous opening Thus, a vicious cycle is established which must inevitably lead to congestive heart failure²

Holman,⁴ and Reid and McGuire⁵ have noted so-called arterialization of the veins and venification of the arteries The former is explained by the increased work and adaptation to heightened pressure, and the latter (venification) is noted as thinning, tortuosity and dilatation proximal to the fistula Because of the fistula and the impaired circulation distal to the opening, intermittent claudication,⁶ chronic ulcers,⁷ engorged veins, and cyanosis of the involved extremity are the rule Bianham's⁵ bradycardia phenomenon (slowing of pulse rate when the fistula is closed) seems directly related to the size of the fistula and the seriousness of the cardiac damage The arteriovenous aneurysm is a powerful stimulant to the development of collateral circulation in the affected extremity, and it is because of this collateral circulation that portions of the artery and vein can be ligated and excised⁶ In young, growing persons there is an actual lengthening of the extremity due to increased vascularity of the growth centers of the long bones,⁶ and this was noted in our case

Case Report—G M, male, age 20, a truck body builder, first presented himself at the Clinic in December, 1936, complaining of a swollen left leg Five years before, when he was 15 years old, he was sitting on the ground playing with a revolver He accidentally discharged the gun and shot himself in the inner side of the left thigh at about the junction of the lower and middle thirds Immediately after the shot he

ARTERIOVENOUS FISTULA

jumped up and ran approximately one-half mile. Then his leg cramped so severely he could run no more. He was carried to a physician's office, and a roentgenogram revealed the bullet lodged in the popliteal space. No attempt was made to remove it. The leg was swollen three or four times its normal size, and it has remained so, more or less, ever since the accident. After a few days the patient was up and about on crutches with his leg in a semiflexed position. Within six weeks he was walking on his toes, and it was several weeks more before he could walk with the heel of the left foot to the ground. Walking a long distance caused cramps in the calf muscles and these ordinarily were relieved if he would sit down and rest.

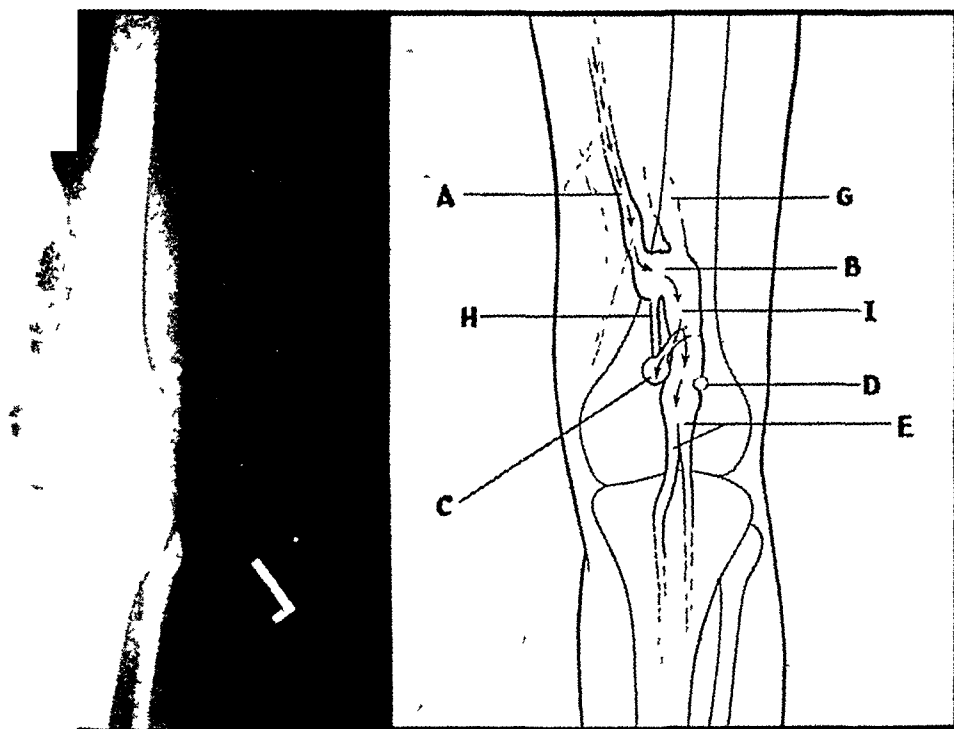


FIG 1—Anteroposterior arteriogram taken immediately after injection of thorotrast. Arrows indicate direction of flow of blood through the fistula. A Popliteal artery above fistula. B Arteriovenous fistula. C Communicating vein. D Bullet. E Branches of popliteal vein. G Popliteal vein above the fistula. H Popliteal artery below the fistula. I Popliteal vein below the fistula.

Subsequently the patient was enrolled at a C C C camp, and when he was given an hypodermic injection of a vaccine for immunization the left leg swelled considerably more than usual. He reported to the medical officer and was sent to an army post hospital for observation, where he was kept 10 days. Roentgenologic studies were made, and he was returned to the camp for duty. A second hypodermic injection of vaccine was given and again the leg became greatly swollen, and this happened a third time following another injection. This great tumefaction persisted for about a week after the third injection and was not altered by overnight rest in bed or by moderate exercise.

The patient first noticed a thrill on the inner side of the left thigh, four or five centimeters above and below the wound entrance, soon after the accident, and it has persisted. This thrill or bruit was not so noticeable to the patient when we examined him as it had been formerly, but we noticed that a distinct vibration occurred with each cardiac cycle. Since the accident the left foot had been warmer than the right foot. All the superficial veins of the left thigh, leg and foot were more prominent than those of the right and had been since soon after the accident.

Physical Examination—This revealed a well-nourished young man, 72½ inches tall, weighing 162 pounds. The blood pressure in the left arm was 140/60. Pulse 100, regular, temperature 98.6°F.

The left thigh, measured at a level five centimeters above the patella, was 10.5 cm greater in circumference than the right. The left leg, measured at a level 20 cm below

the patella, was 77 cm greater in circumference than the right. The left lower extremity was 21 cm longer than the right.

All the superficial veins of the left leg and thigh were prominent. A thrill was palpable on the inner aspect of the left thigh, extending from the wound of entrance down to the knee, and a bruit was heard in the same area. It was much more difficult to feel the pulsations of the left dorsalis pedis artery than of the contralateral vessel.

Roentgenograms of the left knee revealed a foreign body (bullet) in the popliteal space (Figs 1D and 2D). Chest roentgenogram showed the cardiac dimensions near the upper limits of normal (Table II, and Fig 3A).

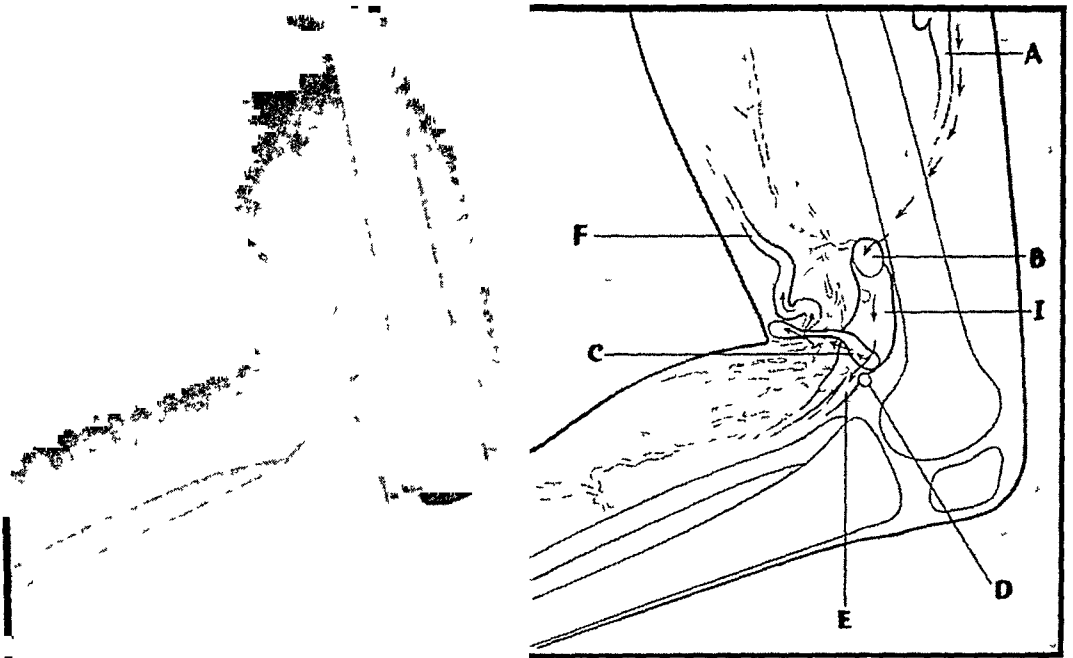


FIG 2—Lateral arteriogram taken immediately after Figure 1. Arrows indicate direction of flow of blood through the fistula. A Femoral artery. B Arteriovenous fistula. C Communicating vein. D Bullet. E Branches of popliteal vein. F Superficial vein. I Popliteal vein below fistula.

A tentative diagnosis of an arteriovenous fistula was made. The gravity of the situation was discussed with the patient and his mother, and it was proposed that further roentgenologic studies with thorotrast injections be made as a guide to proper surgical procedures. Operation was, however, refused, and the patient was not heard from for approximately two years.

On his return most of his symptoms had become aggravated and, in addition, there were two lesions resembling varicose ulcers on the inner surface of the left leg, about four centimeters below the knee. A bruit could still be heard on the inner aspect of the thigh. At this time the blood pressure readings were taken on extremities and are as follows: Left arm 130/60, right arm 130/60, left thigh 140/60, right thigh 130/80. The pulse rate remained 100 per minute. After a blood pressure cuff on the left thigh was inflated sufficiently to close off the aneurysm the pulse rate dropped to 72 per minute within 15 seconds. Thorotrast, (12 cc), was injected into the left femoral artery, using the methods of Yater⁷, and Horton⁸, and roentgenograms were taken (Figs 1 and 2).

Description of Roentgenograms—The first film was obtained immediately after the injection, with the projection anteroposterior. A lateral view was then exposed as quickly afterward as possible. Digital pressure was maintained on the femoral artery throughout these procedures. In spite of this the thorotrast passed rapidly from the arterial to the venous circulation, so that the two views do not demonstrate entirely

the same vessels. The anteroposterior view shows the fistula itself while in the lateral view the tortuous collateral venous circulation is well shown.

The thorotrast can be traced through the fistula as indicated by the arrows in Figs 1 and 2. The popliteal artery (Fig 1A) appears near the inner border of the thigh extending downward and mesially to a level approximately 22 cm above the joint space where the fistula is seen as a rounded collection of dye (Fig 1B). After the dye passes through the fistula into the dilated vein it becomes more dilute and the shadow fainter (Fig 1I). Because of the retrograde flow against resistance the dye concentrates lower down in the popliteal vein, which is particularly well shown with its two branches (Fig 1E). The bullet is seen lodged against the lateral wall of this vein (Figs 1D and 2D). The thorotrast then passes through the dilated communicating branches (Figs



FIG 3—A Chest roentgenogram taken before operation. Area of heart and great vessels 180 sq cm. B Chest roentgenogram taken three years after closure of the fistula. Area of heart and great vessels 135 sq cm.

1C and 2C) to the superficial veins (Fig 2F). The popliteal artery distal to the fistula is barely perceptible as a narrow streak of dye (Fig 1H) because the blood flow is predominantly through the fistula and in a retrograde direction down the vein.

Laboratory Data—Electrocardiogram: Pulse rate 100, sinus tachycardia, moderate right axis deviation. Urine: Negative. Blood: Hemoglobin (S) 93 per cent, erythrocytes 4,500,000, leukocytes 14,000. Kline: Negative. Temperature studies of the extremities with the thermocouple showed a higher temperature in the left thigh, leg, and dorsum of the foot and lower temperature in the left metatarsal area as compared with the right (Table I).

Operation was again offered and was accepted by the patient and his family.

Operation—February 26, 1938, at the Wells County Hospital. Under ethylene, a longitudinal skin incision was made over the popliteal space just lateral to the semimembranosus and semitendinosus muscles. The superficial fascia was incised and the dissection carried down to the aneurysm, which measured approximately 3.5 cm in diameter and was in the proximal part of the popliteal space. The artery was isolated from the opening in the adductors above the aneurysm and down through the popliteal space beyond the aneurysm. The popliteal artery distal to the aneurysm was smaller than proximal to it (0.3 cm distal and 0.5 cm proximal). The popliteal vein was greatly dilated distal to the fistula, and the stream of blood from the opening between the artery and vein could be plainly seen through the vein wall going in a retrograde direction down the vein. The popliteal vein proximal to the fistula was 1 cm and distal it was 2.0 to 2.5 cm in diameter. The popliteal vein and artery lay side by side with

the aneurysm protruding posteriorly. Pressure on the proximal popliteal artery stopped the purr over the aneurysm. The fistulous opening was approximately 0.5 cm in diameter. All four vascular limbs of the aneurysm were doubly ligated with No. 3 chromic catgut after the technic described by Horsley and Bigger.¹ Fascia was closed with No. 1 plain catgut and a rubber dam drain was inserted down to the fistula. The skin was closed with silk.

TABLE I
TEMPERATURE STUDIES WITH THERMOCOUPLES[†]

Area	Before Operation		3 Years After Operation	
	Left	Right	Left	Right
Palm	94.5° F	95.5° F		
Thigh	94.8° F	94.0° F	95.0° F	94.5° F
Leg	96.5° F	93.8° F	96.0° F	96.0° F
Dorsum of foot	86.0° F	85.8° F	91.0° F	90.0° F
Metatarsal	78.3° F	79.2° F	91.0° F	91.0° F

[†] All readings taken at analogous points on each extremity.

Postoperative Course—When the patient entered the hospital his blood pressure was 140/80 and pulse 88. The first postoperative day the blood pressure was 120/80 and pulse 104. On the fourth day the temperature was 98.8°F, pulse 88. The wound was dressed and rubber dam drain removed. At no time in these first four days was there ever any evidence of impaired circulation in the left foot or leg. On the tenth postoperative day the patient was in a wheel chair. The pulse rate varied from 64 to 80. All sutures were removed on the thirteenth day, and the patient was dismissed walking on crutches on the following day.

Subsequent Course—Three years after the operation the transverse diameter of the heart had diminished 2.8 cm and the aorta 0.4 cm. The area of the heart and great vessels was decreased by 45 sq cm (Table II and Fig. 3). At this time roentgenograms showed increased density of the spleen from thorotrast contained in it.

TABLE II
CARDIAC MEASUREMENTS

	Before Operation	After Operation
Transverse diameter of heart	13.6 cm	10.8 cm
Transverse diameter of chest	29.5 cm	29.7 cm
Oblique diameter of heart	14.4 cm	12.4 cm
Area of heart and great vessels	180 sq cm	135 sq cm

TABLE III
OSCILLOMETRIC DETERMINATIONS THREE YEARS AFTER OPERATION

Area	Left	Right
Popliteal area	$\frac{3}{4}$	5
Anterior tibial artery 25 cm below patella	$1\frac{1}{2}$	5

Oscillometric determinations three years after the operation are indicated in Table III. The deep circulation was almost *nil* in the popliteal and anterior tibial arteries. However, the collateral circulation was good as indicated by thermocouple readings taken at the same time (Table I).

DISCUSSION—This case illustrates most of the features seen in an arteriovenous fistula occurring early in life. The affected leg was longer than its fellow, larger in circumference, warmer, and exhibited varicose veins and ulcers. The blood pressure and pulse pressure revealed the expected changes of hypertension, low diastolic pressure and large pulse pressure. The heart was enlarged and Brianham's bradycardia phenomenon could be demonstrated.

It is important as others have noted, that a contemplated operation on an arteriovenous fistula should be delayed until an adequate collateral circula-

tion has been established. This can be determined in part by thermocouple studies of skin temperature. If this instrument is not available, histamine (1 or 10,000 solution) will give almost the same information. In this case a double ligation of each limb of the aneurysm was performed, and the patient has now been perfectly well for three years.

REFERENCES

- ¹ Holsley, I. S., and Biggel, I. A. *Operative Surgery*. C. V. Mosby Co., p. 153, 1937.
- ² Pemberton, J. de J. Discussion, Arteriovenous Fistula. *Proc. of Staff Meet. of Mayo Clin.*, 13, 804, 1938.
- ³ Holman, Emil. *Arteriovenous Aneurysm*. MacMillan Co., p. 40, 1928.
- ⁴ Holman, Emil. Clinical and Experimental Observations on Arteriovenous Fistula. *ANNALS OF SURGERY*, 112, 840, 1940.
- ⁵ Reid, M. R., and McGuire, John. Arteriovenous Aneurysms. *ANNALS OF SURGERY*, 108, 643, 1938.
- ⁶ Heirman, L. G., and Reid, M. R. Management of Arteriovenous Aneurysm in the Extremities. *Am. J. Surg.*, 54, 17, 1939.
- ⁷ Yater, W. M. Thorotrast Arteriography of the Extremities. Report of Illustrative and Unusual Cases. *Am. Heart J.*, 12, 383, 1936.
- ⁸ Horton, B. T. Arteriovenous Fistula Involving the Common Femoral Artery Identified by Arteriography. *Am. J. M. Sc.*, 187, 649, 1934.

SYMPATHETIC DENERVATION LIMITED TO THE BLOOD VESSELS OF THE LEG AND FOOT II

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IN A RECENT preliminary report¹ the anatomic arrangement of the ganglia and rami communicantes of the lumbar sympathetic trunk, as personally observed in the dissecting room, and the surgical application of these observations were presented in considerable detail. The purpose of this communication is to reemphasize, revise, and supplement some of the more important of the originally published observations.

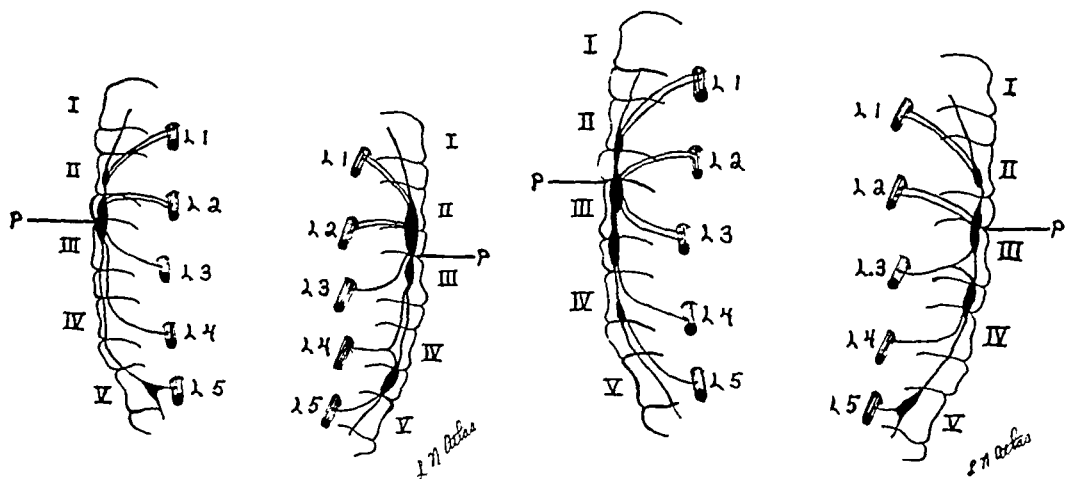


FIG. 1.—Showing some of the typical variations in the topographic anatomy of the lumbar sympathetic trunk. Levels designated by P are the most caudal at which the trunk may be divided without running the risk of obtaining an incomplete denervation of the blood vessels of the leg and foot (ref. Fig. 3).

(1) Because of erratic fusion of lumbar sympathetic ganglionic tissue, it is impossible to designate lumbar ganglia on a numerical basis with any degree of accuracy.

(2) The only lumbar ganglion which is constant in position and connections is that which straddles the second lumbar intervertebral disk, and which is constantly connected with both the second and third lumbar spinal nerves. (This observation has been confirmed by R. H. Smithwick²) Ganglionic tissue connected with the first lumbar spinal nerve may be fused with its rostral pole, and ganglionic tissue connected with the fourth lumbar spinal nerve may be fused with its caudal pole (Fig. 1).

(3) Because of this unpredictable variation in the number and position of the lumbar sympathetic ganglia, it is preferable to describe a lumbar sympathectomy not on the basis of which ganglia were removed, but from the anterolateral surfaces of which vertebral bodies the trunk was resected. This

LUMBAR SYMPATHECTOMY

may be substantiated roentgenographically by placing silver clips on the severed ends of the sympathetic trunk (Fig 2)

(4) Since preganglionic fibers rarely join the sympathetic trunk below the level of the second lumbar vertebra, the simple maneuver of dividing the trunk at the upper pole of the third lumbar vertebra interrupts the flow

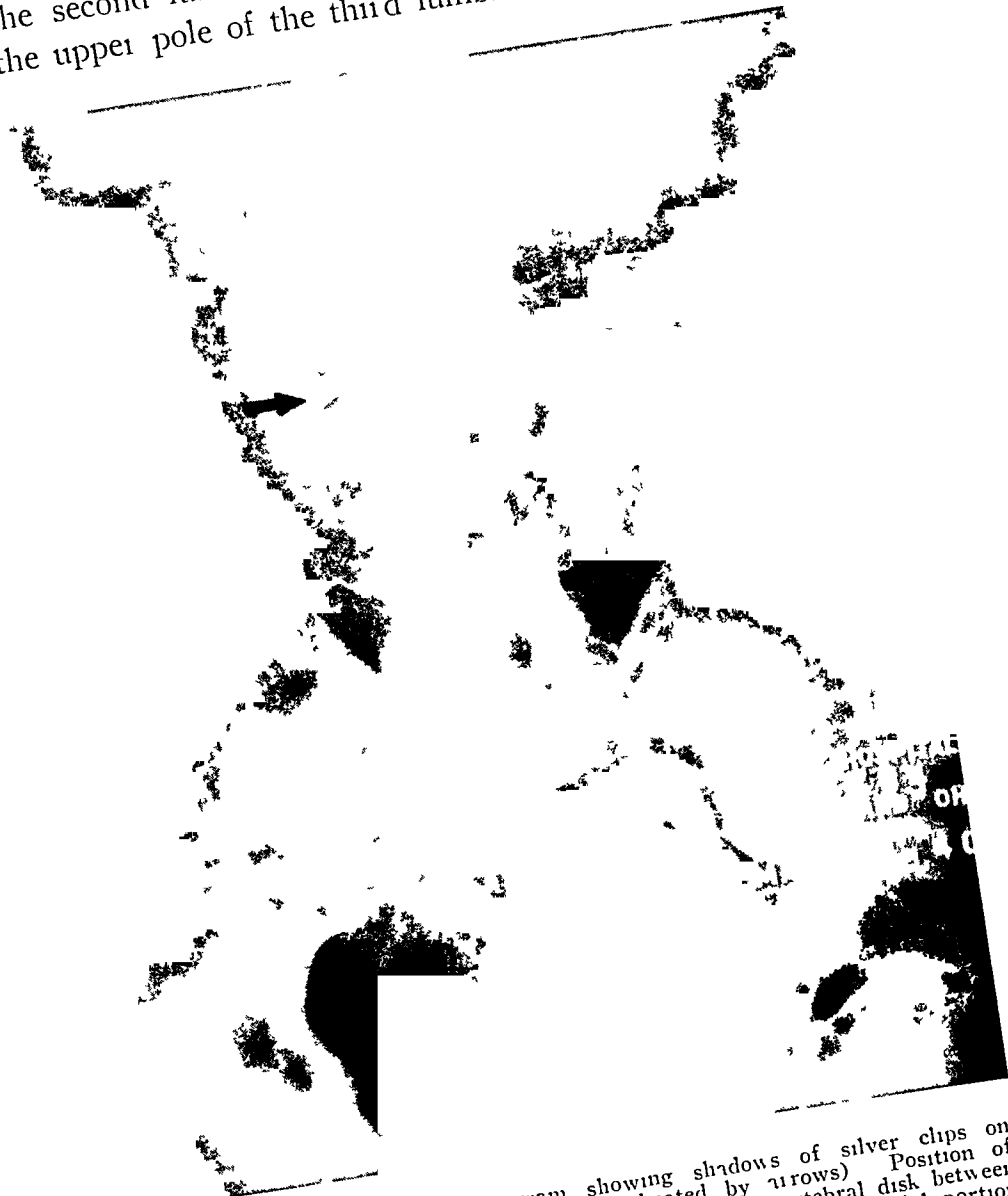


FIG 2—Postoperative roentgenogram showing shadows of silver clips on severed ends of lumbar sympathetic trunk (indicated by arrows). Position of upper clip indicates that trunk was severed at level of intervertebral disk between second and third lumbar vertebrae. Lower clip is point at which caudal portion of severed trunk was buried in the psoas muscle after having been stripped from third lumbar vertebra. (Note sacralization of fifth lumbar vertebra)

of vasomotor impulses to those blood vessels of the lower extremities which receive their innervation through the branches of spinal nerves L 3, 4, 5, S 1, 2, and 3 (Figs 1 and 3). The vessels thus denervated include the popliteal artery and its branches and the cutaneous vessels distal to the thigh. To prevent regeneration, the caudal portion of the severed trunk is stripped for a distance of several inches and, as is technically most convenient, either resected or buried deep in the adjacent psoas muscle. In addition to preventing regeneration, this maneuver also destroys any connections of the trunk with the third lumbar spinal nerve, which might have been

missed when the trunk was divided. This is important in those rare instances in which preganglionic impulses reach the sympathetic trunk over a white ramus from the third lumbar spinal nerve.

At the present time, 68 sympathetic denervations, limited to the blood vessels of the foot and leg, have been performed. This limited type of denervation has proved to be quite adequate for the treatment of Raynaud's disease and other vasospastic dystrophies in which the disturbance was limited to the foot and leg. It has also been found to be of value in the treatment of non-inflammatory obliterating arterial disease of the lower extremity in which an abnormal degree of peripheral vasoconstrictor tone inhibited the development of a collateral circulation.³

In three instances, sweating and vasoconstriction involving the inner border of the lower leg and foot have been observed postoperatively. Roentgenographic check-up of the position of the silver clips revealed that the trunk had been divided at the lower pole of the third lumbar vertebra instead of at the upper pole, thus leaving the postganglionic ramus to the third lumbar spinal nerve intact.

These three cases are considered to be significant because they indicate that sympathetic fibers carried in the branches of the third lumbar spinal nerve may occasionally reach as far distally as the foot. This may explain the empiric observation of Leiche,⁴ and others, that resection of the upper end of the lumbar sympathetic trunk often yields a more thorough denervation of the foot than does resection of the caudal portion. If incomplete denervations are to be consistently avoided, the exposure of the sympathetic trunk must certainly be carried at least as high as the intervertebral disk between the second and

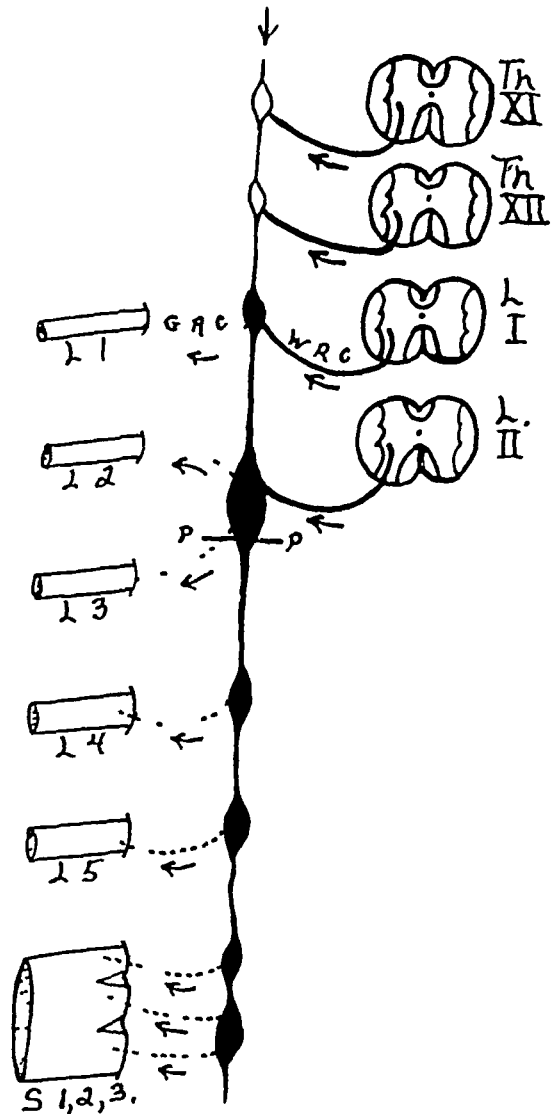


FIG 3—Diagrammatic sketch of pre and post ganglionic sympathetic innervation of the blood vessels of the lower extremity. P—P indicates the point at which the flow of vasomotor impulses is interrupted by dividing the sympathetic trunk at the upper pole of the third lumbar vertebra and stripping the caudal portion from the entire length of that vertebra. Dividing the trunk at a lower level leaves the postganglionic ramus to L/3 intact. Branches of this ramus may reach as far distally as the foot.

Arrows indicate direction of vasomotor impulse flow.

W R C = Preganglionic ramus

G R C = Postganglionic ramus

third lumbar vertebra before the trunk is divided and stripped (Fig 1)

The question arises as to how this particular spot is recognized at operation. It is identified by the presence of the large ganglion which is connected with both the second and third lumbar spinal nerves. It is my practice to carry the dissection upwards until this ganglion is exposed and to sever the trunk through the central portion of the ganglion.

It will undoubtedly be observed by those who have had experience in the field of sympathetic nerve surgery that the technic described is no different from that usually employed. It has not been the purpose of this or the previous communication to offer a new method for denervating the blood vessels of the lower extremity. There are no new methods for accomplishing this end. Rather, the purpose has been to present a clearer appreciation of the precise anatomy of the operation of lumbar sympathectomy.

REFERENCES

- ¹ Atlas, L. N. A Modified Form of Lumbar Sympathectomy for Denervating the Blood Vessels of the Leg and Foot. Anatomic Considerations. *ANNALS OF SURGERY*, 111, 117, 1940.
- ² Smithwick, R. H. Personal communication.
- ³ Atlas, L. N. Lumbar Sympathectomy in the Treatment of Selected Cases of Peripheral Arteriosclerotic Disease. *Amer Heart Jour*, in Press.
- ⁴ Leriche, R. The Surgery of Pain. Williams and Wilkins, Baltimore, 1939.

THE FIFTH BRAZILIAN CONGRESS OF ORTHOPEDICS AND TRAUMATOLOGY

Rio de Janeiro, June 30 to July 3, 1942

Editor's Note —Unfortunately, we received the announcement of this meeting too late to include details of the program in our July issue. However, in the interest of Medicine in South America, we are privileged and pleased to print the following outline of the Congress.

The official reports to be discussed at the Congress are, Obstetric Paralysis and Internal Derangements of the Knee the former having been contributed by Prof. Barros Lima and Dr. Orlando Pinto de Souza and the latter by Prof. Domingos Define and Prof. Achilles de Araujo.

One of the sessions of the Congress will deal exclusively with War Traumatology. Various officials such as officers of the Army's Health Corps, Navy, Aeronautics, Fire Department and State Police having been invited thereto as well as Civil elements. On this occasion Prof. Albee, Honorary Medical Colonel of the American Army and a well known traumatologist will lead a conference.



SYMPOSIUM ON THORACIC SURGERY



CLOSURE OF THE BRONCHUS FOLLOWING TOTAL PNEUMONECTOMY*

EXPERIMENTAL AND CLINICAL OBSERVATIONS

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THE EVER INCREASING APPLICATION of total pneumonectomy to the treatment of malignant and inflammatory diseases of the lung, places on those particularly interested in this procedure the grave responsibility of increasing the margin of safety. The problem considered in our discussion is that of closure of the primary bronchus.

A review of the literature on experimental pneumonectomy impresses one with the fact that, to a great extent, the majority of the authors have had little knowledge of the possible clinical application of the various experimental procedures described. Due appreciation, however, must be accorded those earlier workers whose stimulating reports have given so much impetus to the advances that have been made, not only in experimental but in clinical pneumonectomy, since Gluck's work in 1881. It is, of course, well known that anatomic differences exist between the laboratory animal and the human being which, in large measure, vitiate many of the suggestions that have been made in regard to bronchial suture. On the other hand, the available clinical data on closure of the primary bronchus following total pneumonectomy are very meager, and it is for this reason that we are presenting our observations. We hope that suggestions will be made to aid us in the solution of the problem, and that those whose results have been more successful along these lines will report them. We realize that all too frequently our efforts have been unsatisfactory.

In order to contrast previous experimental observations with our own, we shall present our laboratory data before reviewing the literature. In this

*Read before The American Surgical Association, Cleveland, Ohio, April 6-8, 1942

way the difference in the technic employed in our series of experimental pneumonectomies, and that of others, will be available for a comparative analysis. It is for this reason that we have chosen to reverse the usual order of such a report.

EXPERIMENTAL PNEUMONECTOMY

The various operations were performed under as nearly identical circumstances as possible. Therefore, the same anesthetist (T S), operator (W F R), and assistants (J G, Jr, and I S) carried through all the details of each experiment from the beginning to its final conclusion, thus making for consistency in technic. The dogs were selected to correspond as closely as possible in age and weight, generally speaking, they were young adult animals of medium height, weighing on an average about eight kilograms. A relative uniformity in size and age assures one of a considerable degree of similarity not only in the diameter of the bronchus, but in the flexibility of its walls and the malleability of the cartilaginous rings.

Our experimental observations extend over a period of more than three years, during which time over 200 dogs have been subjected to total pneumonectomy. In addition to the technic which had been employed in the past by various observers, in several of our earlier series recourse was had to methods for the closure of the primary bronchus that had, heretofore, not been used by other investigators. The work of previous authors on experimental pneumonectomy was repeated with, generally speaking, comparable results. It was soon realized that the methods used in the past, in a high percentage of instances, were imperfect, not only in experimental pneumonectomy, but also from the standpoint of clinical application.

After a careful and critical analysis of our operative results and those of previous observers in experimental pneumonectomy, the problem which we faced seemed to be divided into two main parts. First, to develop a method of closure of the primary bronchus of the dog that could be used successfully in a high percentage of experimental pneumonectomies, either for the right or the left side, and, second, that this method should be one that could also be applied to the closure of the primary bronchus in the human being. A review of the literature on experimental pneumonectomy reveals the fact that the great majority of observations made on the closure of the primary bronchus have dealt with the left side. In the dog, as in the human being, the left bronchus, because of its greater length, lends itself more readily to the various methods of closure which have been advocated in the past. On the right side, however, the primary bronchus is very short, consisting, indeed, of only one cartilaginous ring. Because of this shortness a simple circumferential ligature or inversion of the bronchus, after the manner of Willy Meyer, was found not to be a feasible procedure. This anatomic difference has made it impossible to use other proposed methods which could be applied to the left bronchus. In our final series of experimental pneumonectomies the two dif-

ferent methods of closure adopted were workable in the dog, not only for the left bronchus but also for the right

Preliminary Experiments—In successive series of animals, previously reported methods employed in the closure of the primary bronchus were repeated and also certain means of occlusion were tried that had not been utilized by others. Constructing and transfixing ligatures of silk, different sized steel and silver wires, all forms of catgut, silver bands, fascial ribbon alone and in combination with braided silk, were made use of, only to find that in many animals the ligature would cut through the bronchus between the fifth and the tenth day. Particularly was this true on the right side, but regardless of the side the bronchus always opened proximal to the ligature. In a small series of animals the left bronchus was filled with litharge, lead oxide, and glycerine, between two temporary ligatures before the lung was amputated. This substance was injected in a semifluid state by means of the old-fashioned paraffin syringes, and, after setting for a few moments, became rock-like in hardness. After amputation, the bronchus was closed with interrupted sutures distal to the injected mass. A high percentage of the bronchi, occluded in this manner, leaked about the site of injection as the walls dilated about the foreign body. After many other trials the use of interrupted mattress sutures was found to be the most satisfactory method of closure.

Final Experiments—Experimental Operations in the First Series of 36 Dogs Total pneumonectomy was performed in 18 animals on the right side and in 18 on the left side. All animals recovered from the operation, living for a period of over four weeks, and some as long as six months. The series was begun early in the fall. We were fortunate in losing only two animals from distemper but, in all, including the two in which the autopsy findings were typical of distemper with bronchopneumonia, the primary bronchus of the operated side was perfectly healed. The two animals which died of distemper had been operated upon more than two months before death.

A description of a typical experiment is as follows

The animal was given a preoperative injection of 16 mg of morphine hypodermically about one hour before operation. It was anesthetized by drip-ether through an ether cone, until it had reached a sufficient depth of anesthesia to enable an intratracheal tube to be inserted without difficulty. This tube was sterile, and care was taken to avoid, as nearly as possible, all contamination during insertion, and to introduce the tube only part way down the trachea so as to prevent contamination of the primary bronchi. The tube was firmly fixed to the lower jaw by means of a mouth gag and then connected with a continuous flow of air, which by proper adjustment could be completely or partially bubbled through ether. The intratracheal tube being smaller than the trachea, positive intratracheal pressure could be obtained only by the anesthetist compressing the trachea about the tube. A mercury manometer, which constantly registered the intratracheal pressure, was connected with this intratracheal catheter. The side, either right or left, to be operated upon was shaved and thoroughly cleansed with soap and water, then washed with ether, followed by half-strength iodine and alcohol. Great care, from the technical standpoint, was observed in all steps because of the well known fact that the pleural cavity in dogs is easily infected.

An incision was made (Fig 1) over the fourth interspace which, in our experience,

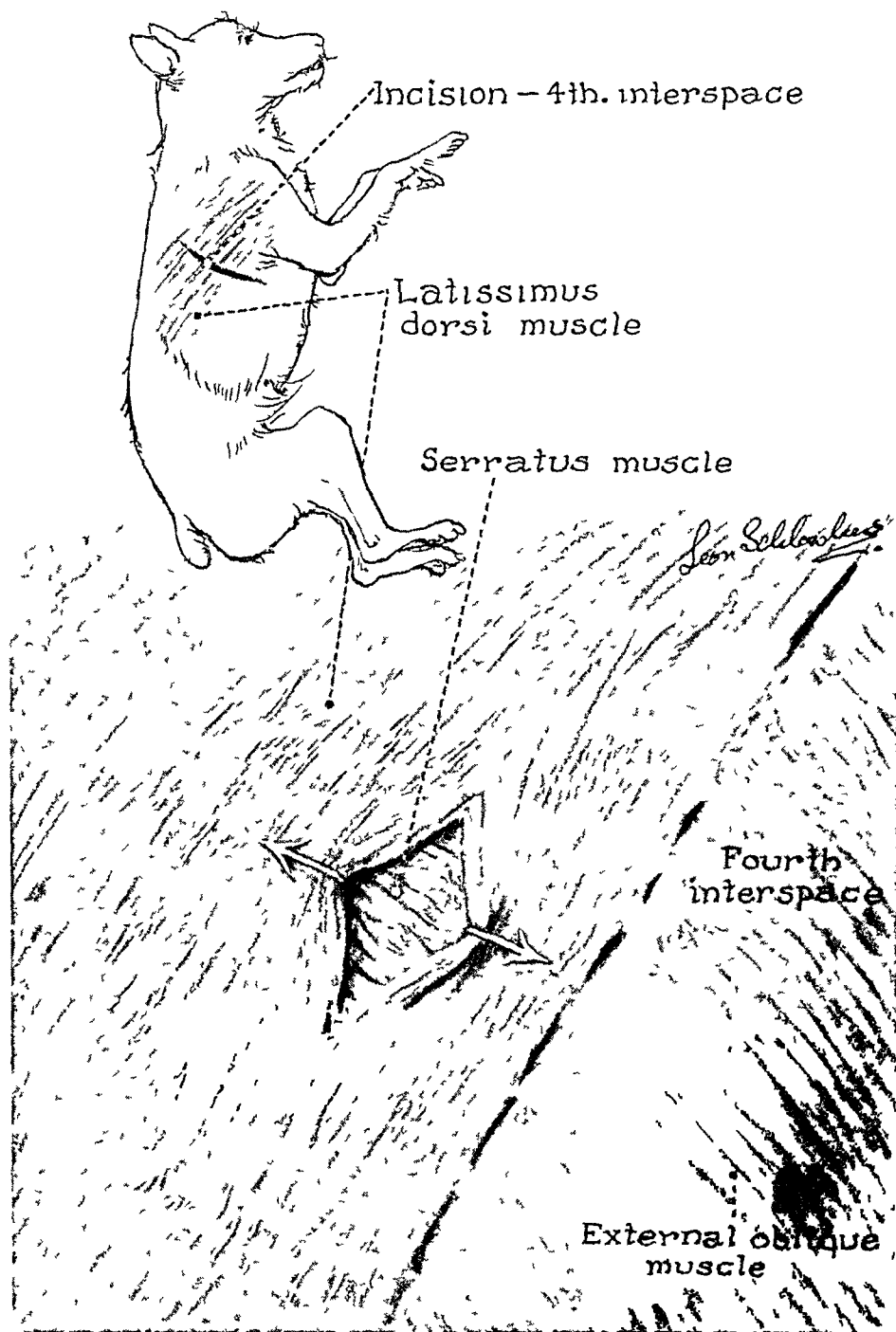


FIG 1—Demonstrating location of skin and muscle splitting type of incision for experimental pneumonectomy

usually corresponded to the point of maximum impulse of the heart and could easily be determined either on the right or left side. The incision usually extended for a distance of about four centimeters on the dome, so to speak, of the chest, about midway between the dorsal and ventral lines. The platysma muscle was cut through along the line of incision. The latissimus dorsi, as noted, was cut along the course of its fibers, which is perpendicular to the incision. The serratus muscle was separated as the incision was carried through the intercostal muscles parallel to the ribs. In this manner, a gridiron

CLOSURE OF BRONCHUS

incision of minimal length was made which caused little damage to the subcutaneous structures when the thorax was entered. After the lung was delivered (Fig 2) the sequence of ligation of the various vessels was slightly different, depending upon whether the right or the left side was operated upon. On the left side (Fig 4), as the pulmonary artery passes over the posterosuperior surface of the left primary bronchus, this vessel was ligated (Figs 2 and 3) and divided. The superior, middle, and inferior pulmonary

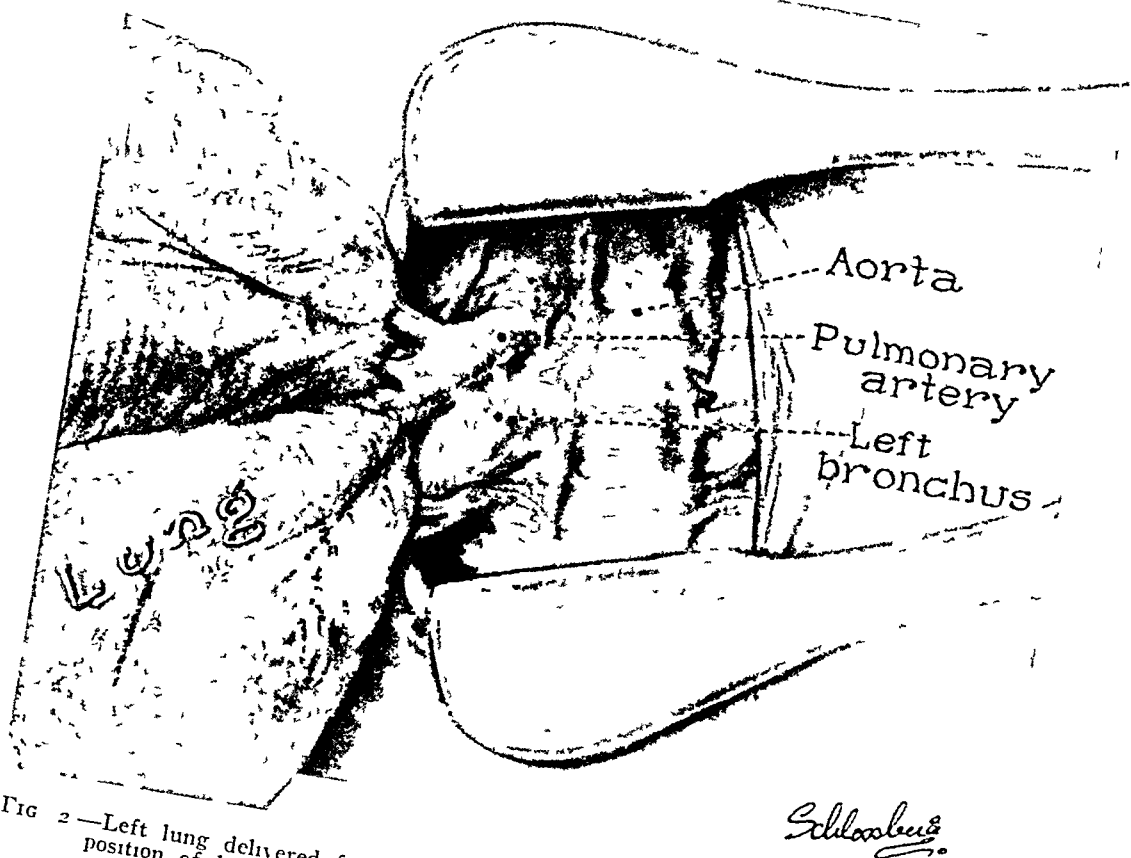


Fig 2—Left lung delivered from thoracic cavity. Note length of left bronchus and position of left pulmonary artery, also type of self retaining retractor

veins were then secured with fine silk ligatures, as were the small arteries on the dorsal surface of the bronchus. The peribronchial areolar tissue on the superior, dorsal, and inferior surfaces was cut across but not dissected back from the proposed line of incision across the bronchus. In nine of the 18 instances, in which the lung was removed on the left side, the bronchus was amputated proximal to the first departing branch, and in the other half at the point of departure from the trachea. Before amputation a row of four to six interrupted mattress sutures was placed postero-anteriorly, each loop of the mattress suture, encircling one cartilaginous ring. Thus the posterior membranous portion was made to approximate the anterior cartilaginous rings and the amputated end of the primary bronchus was flattened (Fig 4).

It is to be recalled that in the dog the bronchial rings form more of a complete circle than in the human being, and in order to fit the posterior membranous portion into the arch of the anterior cartilaginous ring in the dog the most ventral ends of these rings must be angulated upon themselves and approximated to the anterior portion (Figs 4 and 5). This is not true of the human being, where the ring forms more of a semicircle. However, one row of interrupted mattress sutures was so placed and then the bronchus amputated beyond this suture line. It is to be noted that there was no crushing of the bronchus with clamps nor was any chemical or thermal cautery used

nor any attempt made to destroy the mucosa either under the suture line or distal to it. The intratracheal pressure at this point was always increased to at least 80 Mm of pressure, which caused a hyperexpansion of the lung on the unoperated side. This hyperexpansion would invariably demonstrate the fact that the amputated bronchial stump was sealed airtight by the sutures. If by any chance there was some hissing or other evidence of leaking air, another interrupted mattress suture was inserted. The mediastinal pleura was then sutured over the amputated end of the bronchus with a few interrupted silk sutures covering the raw surface of the operative field in order to render the operation a more finished procedure. The routine closure of the chest was accomplished by the use of two pericostal sutures of No. 10 braided silk (Fig. 6) which were drawn home and tied as the anesthetist expanded the contralateral lung, expelling as much air from the thorax as possible. Two, or at the most three, interrupted silk sutures were employed to close the opening in the latissimus dorsi and a continuous subcuticular and cuticular silk suture was used in the skin. No dressing was applied to the wound (Fig. 7). Silk sutures were used throughout.

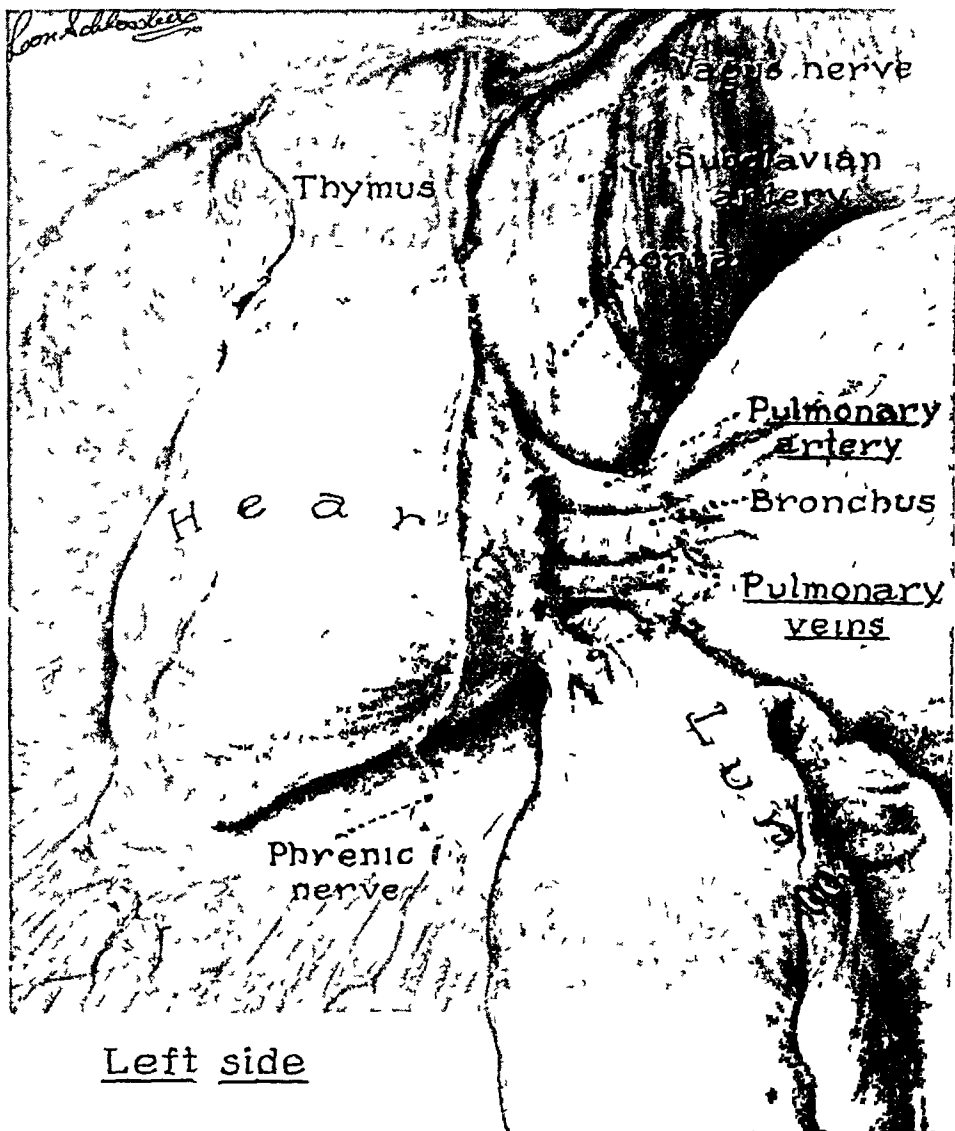


FIG. 3.—Anatomic demonstration of ventral surface of left lung, showing the hilar structures

CLOSURE OF BRONCHUS

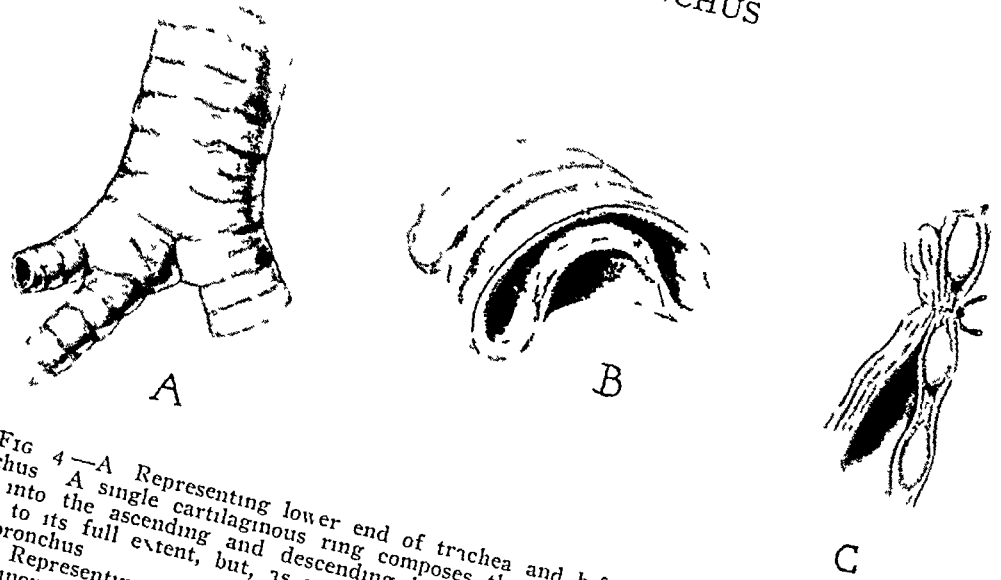


FIG 4—A Representing lower end of trachea and bifurcation into right and left bronchus. A single cartilaginous ring composes the right main bronchus which bifurcates into the ascending and descending branches. The left bronchus has not been drawn to its full extent, but, as indicated, is longer and smaller in diameter than the right bronchus. B Representing cut end of bronchus, demonstrating the extent to which the cartilaginous rings almost completely surround the bronchial tube, forming more than a semicircle with a small posterior membranous portion, less than in the human being. C Method of closure of dog's bronchus with interrupted mattress sutures, opposing posterior membranous to anterior cartilaginous portion.

The operation on the right side differed from that on the left only insofar as the sequence of ligation of the pulmonary vessels was concerned (Fig 8). It is somewhat easier on the right side to ligate first the upper and middle pulmonary veins before attempting to tie the pulmonary artery. The latter lies deeper on the ventral surface and can be readily secured after the veins are ligated. The treatment of the bronchial stump was the same as on the left side.

Due to the fact that the right primary bronchus consists of only one tracheal ring, the use of interrupted mattress sutures for experimental, total right pneumonectomy proved to be a most satisfactory method. It is impossible, even in the dog, to invert this stump or to use a circumferential ligature on it, as the latter will invariably cut through because of tension.

The dogs were returned to the cages always in excellent condition. There was occasionally some hyperpnea following operation, but very little. The animals were placed on a regular diet the following day. Except for the two that died of distemper, there were no fatalities.

The length of time consumed in these experimental pneumonectomies was never over 20 minutes. The same instrument table was used at each operative session, at which time a minimum of two dogs were always operated upon, one on the right side and one on the left side.

Roentgenograms of the chest were taken 24, 48, 72, 96, and 120 hours following operation to determine the rapidity of the compensatory dilatation of the remaining lung, manifested by pushing of the heart and the mediastinal structures to the operated side, with subsequent obliteration of the dead space resulting from the removal of one lung. In all instances, after 48 hours, the heart was completely displaced to the chest wall of the operated side. In some animals this occurred in 24 hours. There was never an accumulation of fluid in the chest of the operated side, and no instances of infection of either

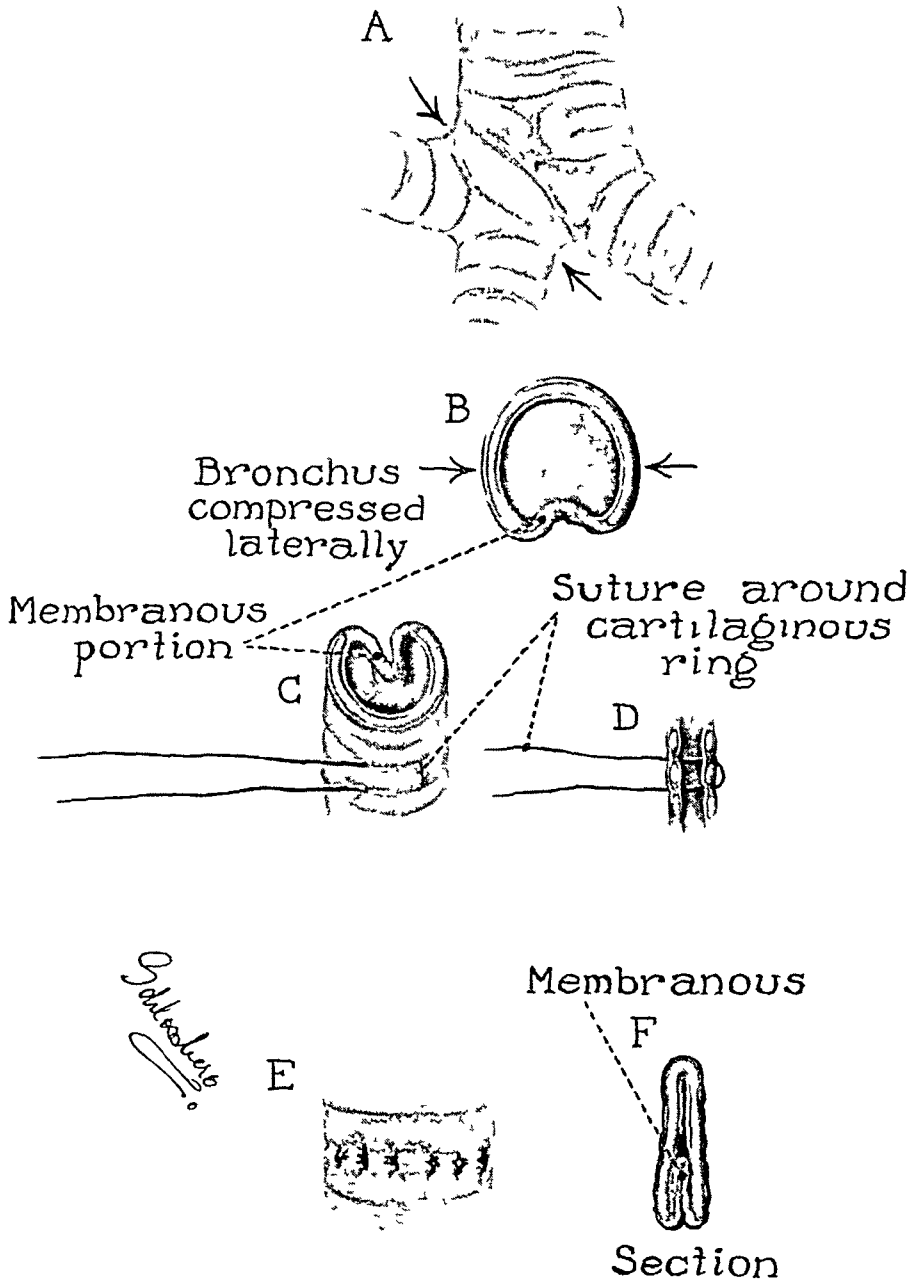


FIG 5—A Demonstrating the relative length of the right and left bronchus. The right is seen to be composed of a single cartilaginous ring.

B Cross section of bronchus, again showing the proportion of the membranous to the cartilaginous portion.

C Insertion of mattress sutures laterally so as to compress the walls of the bronchus laterally instead of anteroposteriorly.

D, E, and F The completion of this approximation.

CLOSURE OF BRONCHUS

Fig 6—Closure of the thoracic cavity with pericostal sutures

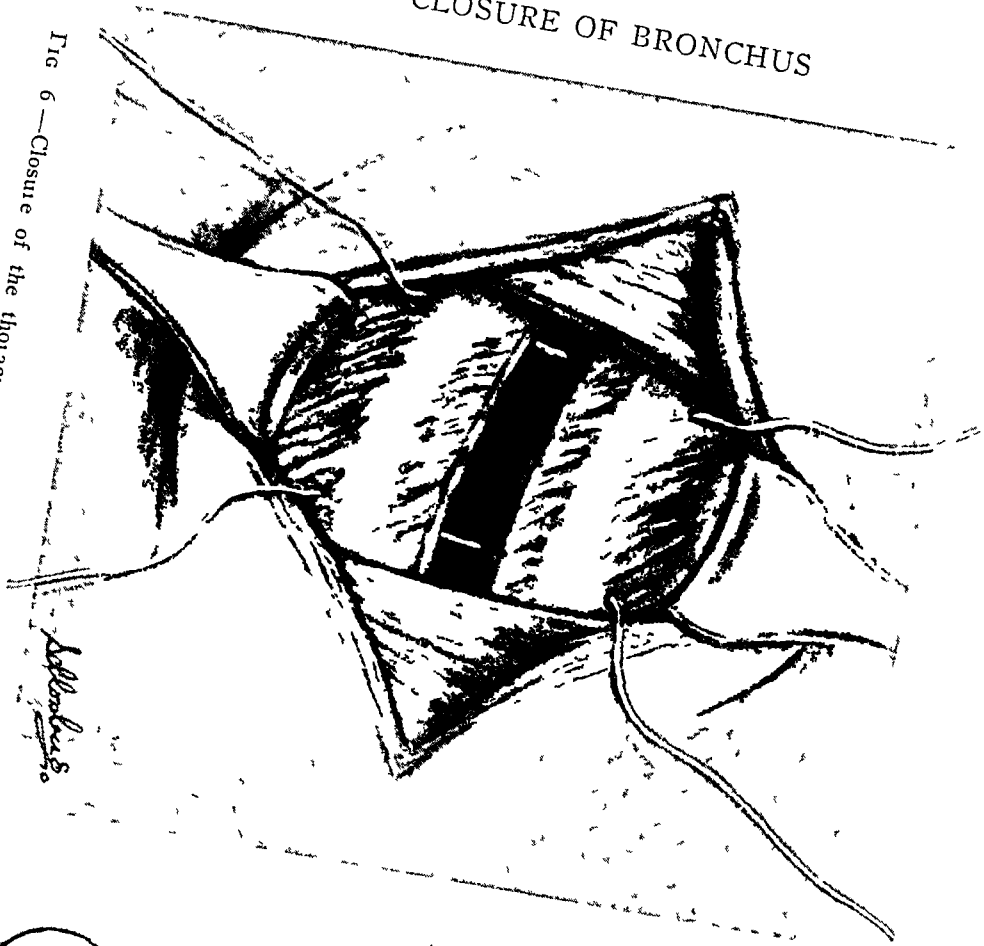
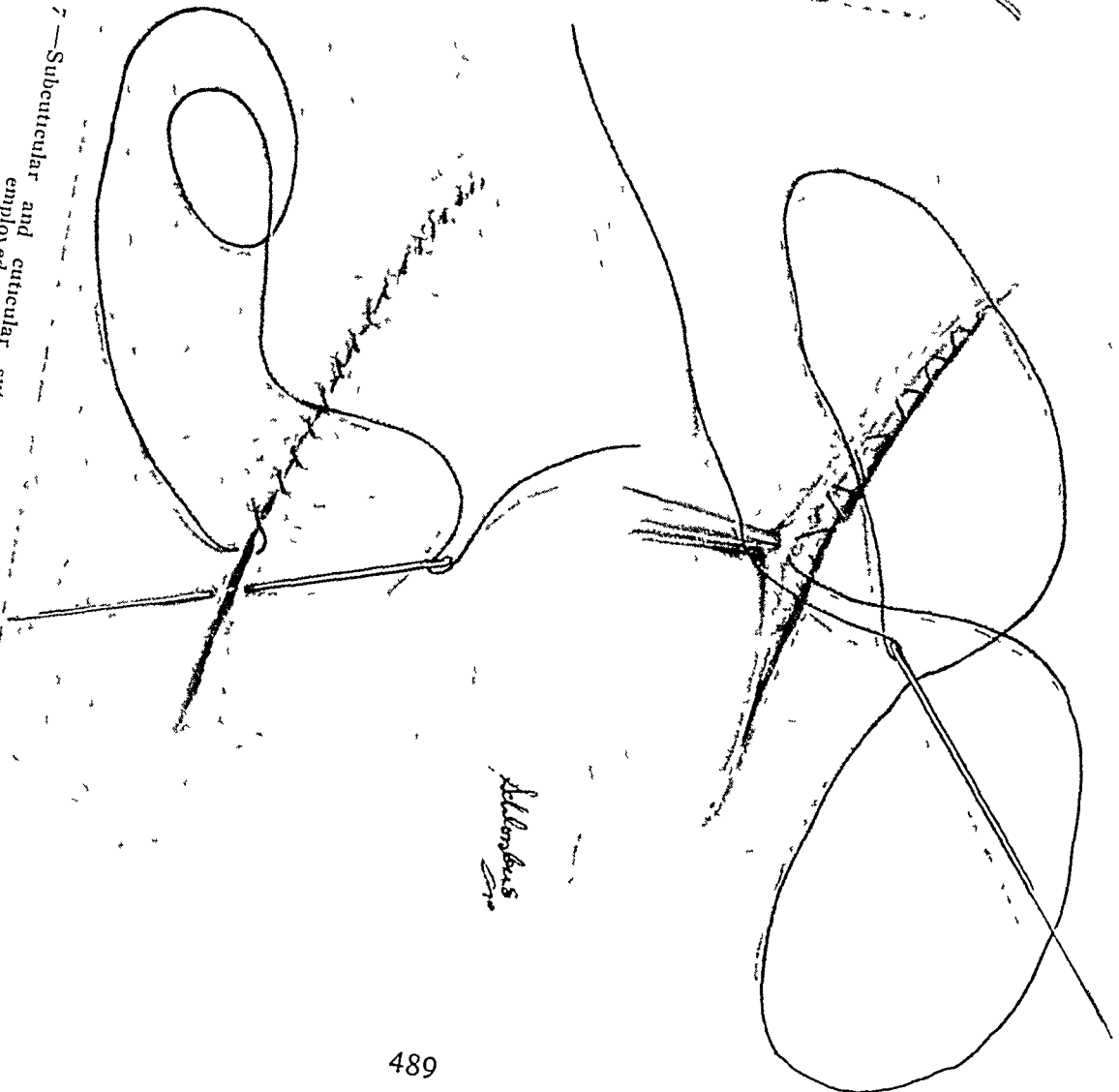


Fig 7—Subcuticular and cuticular sutures in the skin. Actual length of incision employed is of the same length as illustrated



the wound or the pleural cavity occurred in the entire series. From time-to-time Dr E. N. Broyles performed bronchoscopic examinations on various animals and made lipiodol bronchograms, which showed complete healing of the bronchial stump.

In this series, no animals were sacrificed in less time than four weeks, and some were allowed to live as long as six months. On account of the shortage of cage space and the expense of keeping the animals, there was a necessity for sacrificing them within a reasonable time after operation when the bronchus was unquestionably healed solidly. After lipiodol bronchograms had

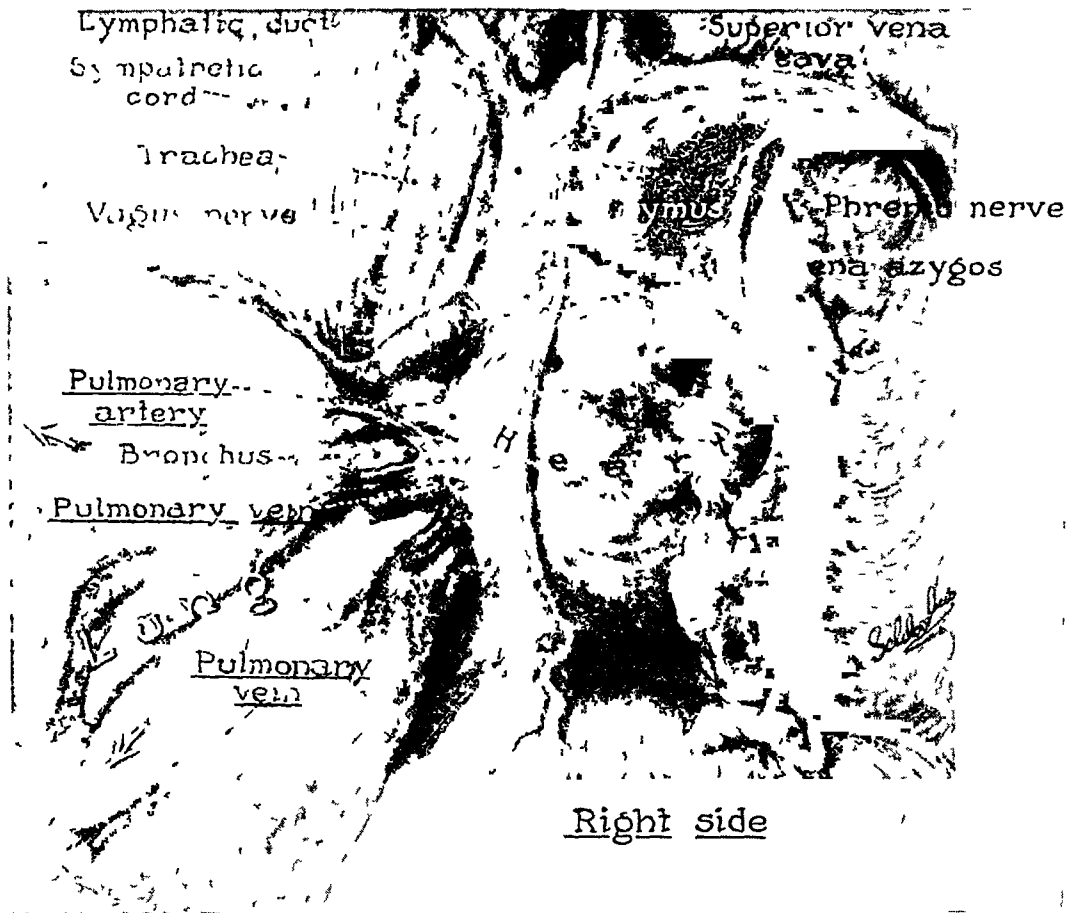


FIG 8—Anatomic demonstration of the right thorax, mediastinum and hilus of right lung in the dog

been made of each animal they were sacrificed in a routine manner. The chest was opened on the operated side and filled with water. With the tracheal tube in place and connected with a mercury manometer the intratracheal and bronchial pressure was raised to 200 Mm. of mercury and in some instances to 300 Mm. There was of course, a hyperdistension of the remaining lung. Due to the fact that the healed bronchial stumps were under water, any bubbling of air could be readily detected. There was no instance in this series in which the bronchial stump leaked.

It is to be noted, here, that a pressure of from 8 to 10 Mm. of mercury

would distend the unoperated lung to its maximum capacity at the completion of the operation. This fact was determined by inflating the lungs of animals in earlier preliminary experiments. The amount of pressure necessary to fill the chest depends, of course, on the size of the dog, but as stated in the beginning, our dogs were more or less of uniform size and weight so that an average pressure required for such distention could be determined within

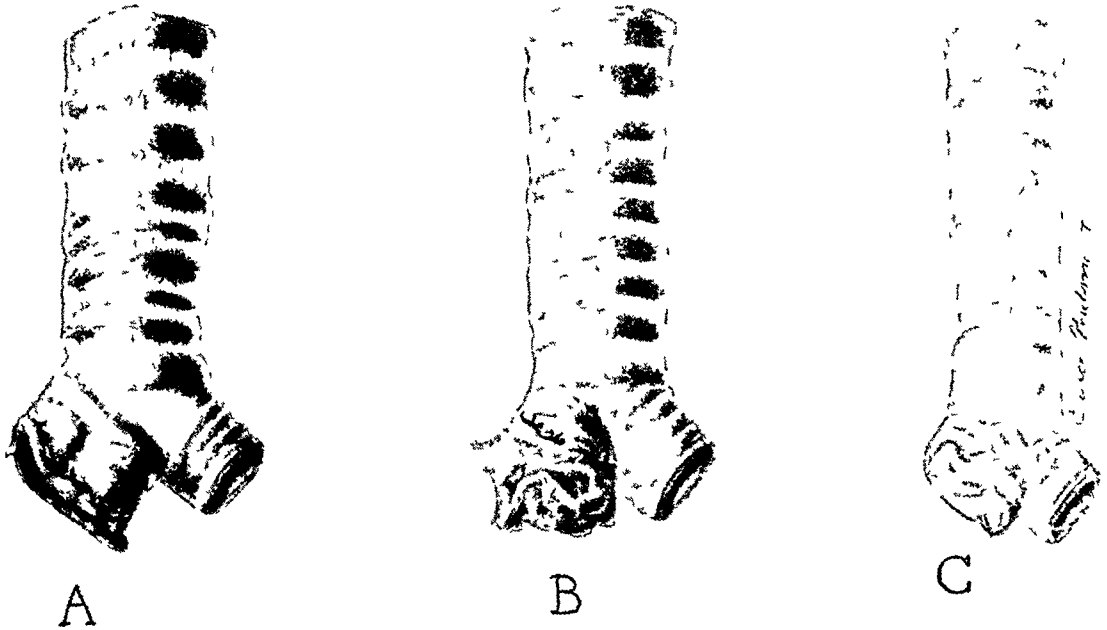


FIG 9—Illustration of gross specimens dissected at autopsy, showing three distinct types of healing encountered after suture of the bronchus, as described in the first series of 36 dogs

- A The conical shaped bronchus that has healed as it was sutured at operation
 B The sutures have cut through the wall and the open end is healed with a fibrous tissue mass. Sutures may be seen to lie in the peribronchial tissue
 C Sutures have cut through, evidently discharged into the lumen of the bronchus. No evidence of them in the peribronchial tissue. Walls of bronchus completely separated and cut end of stump healed over by membranous sheet of tissue

reasonable limits. The healed bronchial stumps were carefully dissected and preserved in either formalin or van de Grift's solution. Serial sections were cut and stained with hematoxylin and eosin.

Experimental Results in the First Series of 36 Dogs—These showed plainly, in the gross, that on the operated side the mediastinal pleura was everywhere smooth and glistening and that only a slight dimpling, when a pull was made on the trachea, revealed the buried healed stump of the bronchus. In every instance the mediastinal pleura had healed completely with an almost invisible scar. In all specimens the bronchus formed a rounded stump covered externally with fibrous tissue. When the internal surface of the healed bronchial stump was examined it was at once noted, from the gross appearance, that the healing differed. In only 18 per cent (Figs 9 and 10) was the bronchial stump conical in shape, with the appearance of being healed as it had been sutured at the time of operation, the tip of the cone being at the point of approximation of the anterior and posterior surfaces. This was considered the ideal type of healing. In another small group, 16 per cent, the

lumen of the bronchus appeared undiminished to the end, across which there was a flat membrane that completely closed the cut end of the bronchus, very much as the skin covers a drum. It was noted also, that in these instances there seemed to be a central elevation with two lateral depressions at the healed end as one viewed the bronchus from the inside, as shown in Fig 10. This elevation appeared to bisect the membrane extending across the circumference of the bronchial lumen with two pits on either side. In nine per cent the end of the bronchus seemed to be filled with a mass of fibrous tissue the inside surface of which was very irregular and resembled, at times papilloma-like formations (Fig 10).

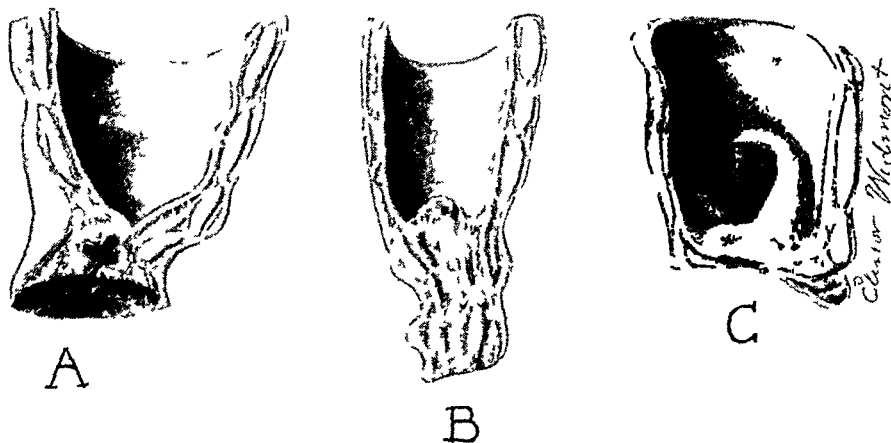


FIG 10.—Cross section of gross specimens shown in Fig 9 A B and C

A Bronchus healed as sewn at operation

B Walls of bronchus separated as a result of cutting of silk sutures and open end healed by the formation of a fibrous tissue plug or mass occluding the lumen. The internal portion of the mass is covered with bronchial epithelium

C Sutures have cut through in the lumen two mounds may be seen. Bronchial walls have separated and the open end has been occluded by a thin membrane stretching between the cut cartilaginous rings. Internal surface of cylindrical end irregular with elevated ridges flanked by depressed areas on either side of ridge

In the majority of animals, 57 per cent, the manner in which the bronchial stump healed proved to be a combination of the three types mentioned above. From the gross appearance the bronchus would be conical in one portion of the healed end while the remaining half appeared to be blunt or rounded and covered over by a thin membrane. In instances in which the bronchus was not entirely conical but had healed partially as sewed, silk sutures were usually visible beneath the lining epithelium of the internal surface of the bronchial stump, and were always proximal to the healed edge of the bronchus. In several instances these sutures had ulcerated part way through the lining epithelium of the bronchial stump, but had not been discharged. Some were nearer the healed end than others, but all were proximal to the ultimate line of healing (Fig 10). The internal surface of some of the healed stumps, that were not conical but rather cylindrical, was often indented by small tangential bands or ridges (Fig 11) as though the epithelium had grown over

some protruding mass that had plugged the end of the bronchus. Sections through various diameters of the bronchi were cut *seriatim* so that a microscopic study could be made of the different types of healing. From a study of the microscopic sections it was found that the bronchi had healed, as anticipated from an examination of the gross specimens, in a manner that permitted classifying them into four main groups. First, the ideal or conical type, in



FIG 11.—Inner surface of amputated stump of right bronchus (dog sacrificed after four weeks) shows epithelization having occurred over irregular internal surface of fibrous tissue mass occluding the end of the bronchus.

which the bronchus had remained closed as sutured at operation and in which all sutures had remained in their original position without cutting through (Fig 12). This group comprised 18 per cent of the animals. The second division included 16 per cent, in which all the sutures had cut through and the bronchus had opened completely. The cut end had been closed only by a membrane which was composed of bronchial epithelium and subpleural and contiguous areolar fibrous tissue contributed by the bronchial wall itself (Fig 13). In nine per cent there appeared to be a firm connective tissue plug which filled the end of the bronchus, the sutures as placed at operation had cut through, the bronchial walls had separated, and the portion of the bronchus distal to the suture line was closed by means of this tampon (Fig 14, a and b). This consisted of white fibrous connective tissue, capillaries, and lymph follicles, as well as apparently atrophic, nonviable portions of cartilage forming part of the bronchial wall distal to the row of mattress sutures. In the peribronchial portion of this mass of fibrous tissue encysted silk sutures were often found. These probably were those mattress sutures which had cut through the walls of the bronchus, but had not ulcerated into the lumen and hence were not coughed up. Such cysts consisted of small abscesses lined

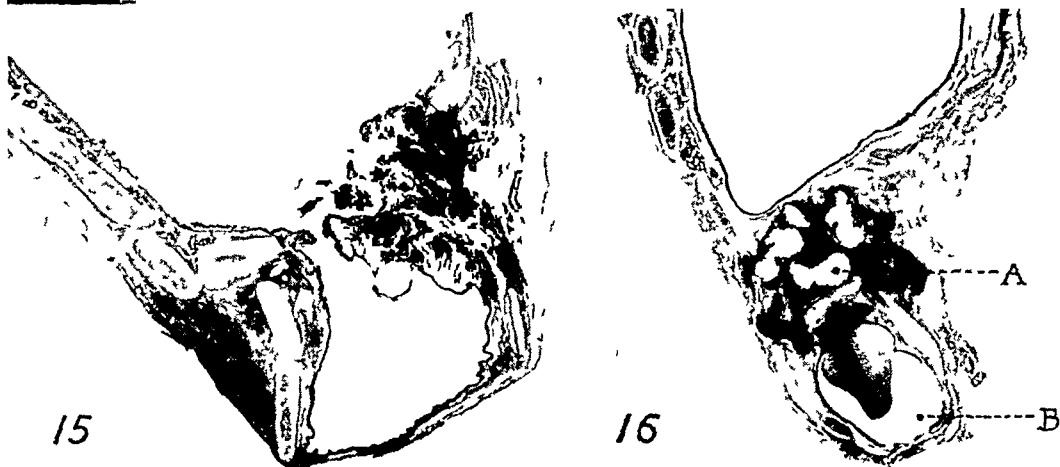
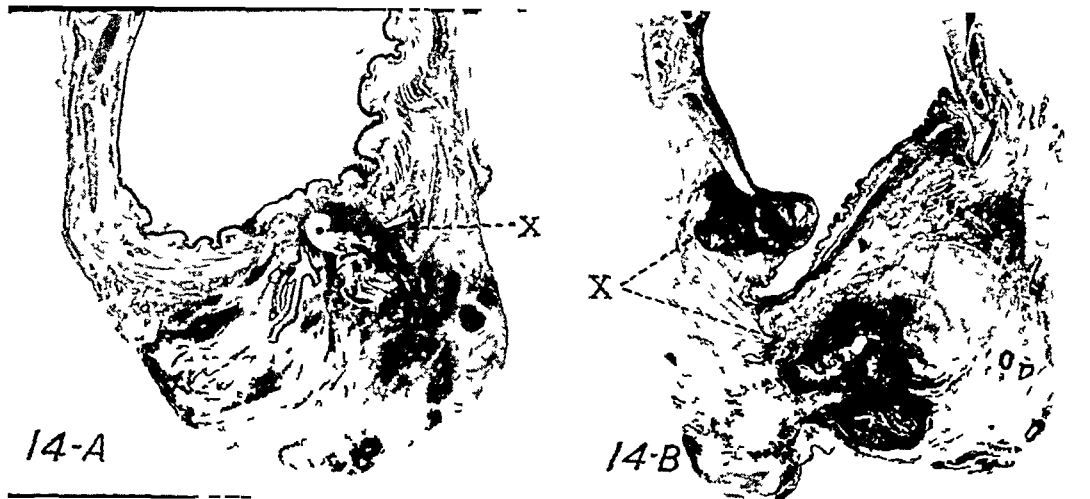
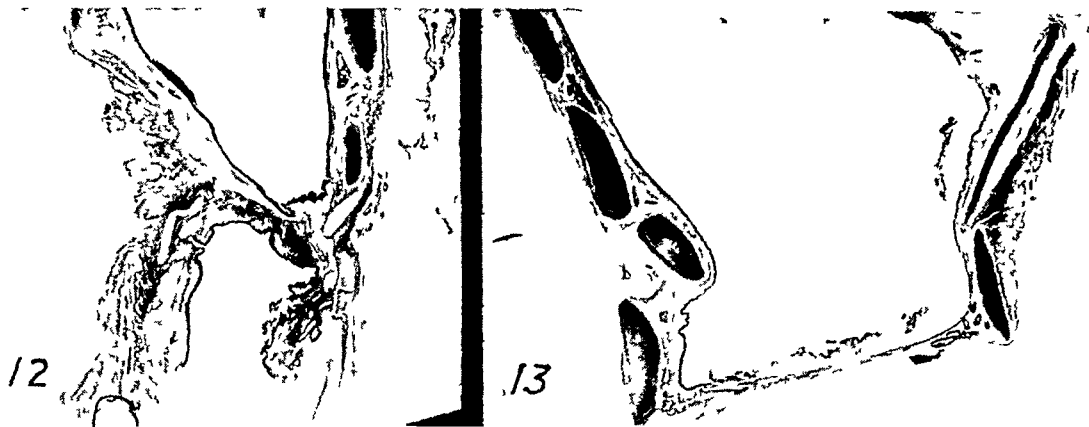


FIG 12—Dog A 2 (section 8 micra, \6) Dog sacrificed after four weeks. Conical bronchial stump healed as sutured at operation. Note viable bronchial cuff distal to healed stump. Ideal type of healing such as this occurred in only 18 per cent, shown in gross (Figs 9 and 10A)

FIG 13—Dog A 3 (section 8 micra, \5) Dog sacrificed after four weeks. Type of healing shown in gross specimens (C of Figs 9 and 10). Bronchial walls opened, healing occurred at end of amputated stump. Note flattened regenerated epithelium and absence of mucous glands in the portion of the occluding membrane that has been driven from subpleural and bronchial connective tissue

FIG 14—A Dog A 23 (8 micra, \6) Dog sacrificed after four weeks. Healing of bronchial stump has occurred as in Figs 9 and 10, Type B. Silk sutures have cut through and shown at X to lie in a cyst like microscopic abscess. Note the bronchus occluded by fibrous tissue mass

B Dog A 27 (8 micra, \5) Dog sacrificed after four weeks. Cutting silk sutures seen at Y. Fibrous tissue mass has plugged end of bronchus through which epithelium has grown. Bronchial walls had opened widely as a result of cutting silk, one suture being extruded into lumen

FIG 15—Dog A 9 (8 micra) Dog sacrificed after two months. Shows lumen of bronchus almost completely closed by diaphragm of bronchial wall at the site of the suture line. However sutures have cut through, one may be seen in the lumen above diaphragm. Bronchus healed at cut end by membrane derived from bronchial and subpleural connective tissue. Open communication between lumen of main bronchus and cut end

FIG 16—Dog A 2 (8 micra, \6) Dog sacrificed after eight weeks. Shows cylindrical stump of bronchus healed by fibrous tissue plug with two forms of cysts. First microscopic abscesses containing sutures which have cut through the wall and separated the healed stump of bronchus from the remaining viable cuff which has in itself healed and formed a cyst like structure lined with bronchial epithelium. The microscopic abscesses are labeled A, and the cyst formed from the cuff of bronchus distal to the suture line is labeled B

mainly with small and large mononuclears, some giant cells, and polymorphonuclear leukocytes. There were also some cysts which were lined with bronchial epithelium that probably represented the epithelial lined portion of the bronchus which lay distal to the suture line. This epithelium seemed to persist whereas the cartilage appeared to atrophy.

In 57 per cent the healing of the bronchus took place in a manner that might be considered a combination of the above described three main types. Part of the bronchus would be healed as sewed at operation while another part might be filled with a fibrous connective tissue plug over which the epithelium had grown and had occluded the bronchus. Another combination proved to be one in which a portion of the bronchus had opened while a small part that had healed as sutured remained as a persistent shelf. In some sections this shelf would almost but not quite cover over the lumen of the bronchus, leaving a small opening into a cyst-like structure distal to the original suture line. This cyst-like structure had been formed by the apposition of the mediastinal pleura and fibrous tissue across the open end of the distal cuff of the bronchus (Fig 15). The various combinations of this type of healing are shown in Figures 14 A and B, 15, and 16.

This series, therefore, demonstrated to us that, regardless of the perfect end-results of the experiments as far as the survival of the animal was concerned, and despite the care in the technic as well as in the method of suture, there will be a high percentage of animals in which the bronchus will open entirely, or in part, because of cutting through of the sutures, and that one could not depend upon either the type of suture or the method of its insertion to close the bronchial stump completely and permanently. In this series of experiments, had it not been for the fact that the mediastinal pleural and also the peribronchial connective tissue had participated in the closure of the bronchus, there would have been many instances in which the bronchus would have leaked and the animal would have succumbed.

It was concluded from this series of experiments that the technic of closure of the bronchus should comprise the general surgical principles of the minimum of trauma and the maximum of preservation of the viability of the tissues. Healing of the bronchus is mainly accomplished by a proliferation of peribronchial and submucosal fibrous tissue together with a growth of granulation tissue derived from the nonserous surface of the mediastinal pleura. An additional contribution made by the bronchus is the layer of epithelium which seems to be very vigorous and needs only a viable base upon which it may grow. This viable base may be supplied by an occluding mass of granulation tissue in the mouth of the bronchus or a delicate layer derived from the nonserous surface of the mediastinal pleura.

Experimental Operations in the Second Series of 48 Dogs—It occurred to us that it would be interesting to determine whether healing of the amputated bronchial stump would take place if only the mediastinal pleura was sutured across the cut end of the open bronchus, without any attempt to close this open end with either suture or ligature. Accordingly, a series of 48 dogs

were operated upon, the right and left side alternately, thus affording 24 instances of right total pneumonectomy as well as left. In this series there were two deaths from distemper at the end of two and one-half weeks, in both instances the bronchus was completely healed and the lesions of distemper were present and typical.

In this series of 48 animals, 36 were allowed to live more than four weeks, excepting the two that have been mentioned as having died of distemper, while ten were sacrificed after 24, 48, 72, 96, and 120 hours in order to determine the amount of increase in intratracheal pressure that the recently closed bronchus would withstand.

In previous experiments in which the lungs were distended with air in both living and dead animals it was found that an increase in intratracheal pressure up to 10 mm. of mercury could cause an expansion of the lungs sufficient to fill the thoracic cavity completely.

In 26 animals of our second series following total pneumonectomy, intratracheal pressure readings were recorded at the time of the completion of the operation and when the animals were sacrificed. Immediately following total pneumonectomy the contralateral lung was routinely overdistended, in order to ensure proper oxygenation as well as to secure apposition of the cut end of the bronchus to the mediastinal pleura covering this end. It is to be recalled that the dogs used were of as nearly uniform weight as possible, averaging about eight kilograms. To our surprise, the mediastinal pleura would not allow the escape of air from the open end of the bronchus until the intratracheal pressure was above that required to hyperdistend the unoperated lung. The escape of air was recognized by a faint hissing sound audible at the time of operation. The lowest pressure withstood at the completion of the operation was 12 mm., the highest 50 mm., and the average 24 mm. In this second series of 26 animals sacrificed after four weeks the bronchi withstood intratracheal pressure up to 300 mm. without leaking. The readings were made with the healed end of the bronchus under water. Since above 300 mm. of mercury pressure the unoperated lung will rupture in some areas, this figure was considered evidence of complete healing. In ten instances the animals were sacrificed after 24, 48, 72, 96, and 120 hours following operation. In two in which the postoperative duration of life was 24 hours, the pressure endured at time of operation was 12 mm. whereas the postmortem pressure was 300 mm. Three animals sacrificed after 48 hours advanced from operative readings of 12, 10, and 20 mm. to 300, 200, and 80 mm. The remaining five dogs revealed almost identical readings. Two of them were killed after 72 hours and the remaining three at the end of 120 hours. The operative pressure sustained was between 30 and 40 mm., whereas the bronchi did not leak when the intratracheal pressure was run up to 300 mm. at the time the animals were sacrificed. This unexpected tenacity of the open cut end of the bronchus to the overlying mediastinal pleura and areolar tissue depends primarily, as will be demonstrated, upon the presence in the end of the bronchus of a fibinous and later a fibrous plug, and, secondarily,

upon the apposition of the end of the amputated bronchus to the nonserious surface of the mediastinal pleura. The constant hyperdistention of the remaining lung maintains the open bronchial tube in constant contact with the covering alveolar tissue.

In 30 animals in which cultures were made from the primary bronchus at the time of operation, 18 were infected, *B. bronchisepticus* was present in

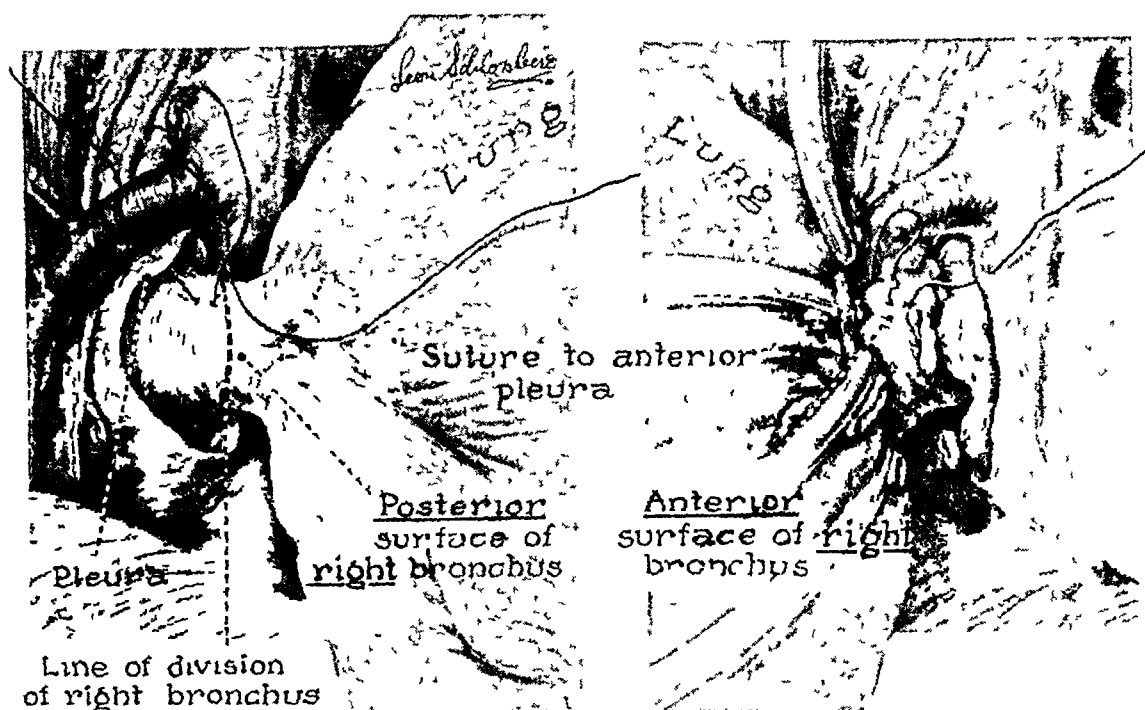


FIG. 17.—Illustrating a method of placing presection sutures before amputation of right primary bronchus in type of closure used in second series of experimental pneumonectomies. Azygos vein may be seen at upper portion of primary bronchus.

11, *B. subtilis* in five, and *Staphylococcus albus* or *citreus* was grown with *B. anthrax* and *B. coli* in one each.

The technic employed in these experiments was as follows:

The total pneumonectomy was performed just as in the first series of experimental pneumonectomies, except that no suture was used to close the end of the bronchus on either the right or the left side. The nonserious surface of the mediastinal pleura was sutured across the opening of the proximal end of the amputated bronchial stump. This was accomplished by means of interrupted presection silk sutures through the lips of the incised mediastinal pleura from the posterior to the anterior aspect of the bronchus, at the same time a very small bite of peribronchial fibrous tissue was taken on the posterior and the anterior surface of the bronchus so that the mediastinal pleura would be held snugly against the cut open end of the bronchial stump (Figs. 17 and 18). Three such sutures were placed and the bronchus was amputated. Since the animals, of course, cannot breathe until the sutures are tied and the edges of the mediastinal pleura approximated over the cut end of the bronchus, as little time as possible must be consumed in performing this type of operation.

On the left side, three pleural sutures usually sufficed, on the right side, sometimes an additional stitch and occasionally two were required. In not one instance was any difficulty encountered in securing close apposition of the mediastinal pleura to the cut end of the bronchus. The anesthetist, by increasing the intratracheal, and thereby the intrapulmonic pressure in the unoperated lung, caused an immediate hyperdistention of

the remaining lung which resulted in displacement of the film-like mediastinal pleura and hilar structure to the operated side. Thus displacement, by virtue of its force alone, brought the end of the bronchus in close apposition to the mediastinal pleura. However, in order to ensure a snug approximation of this pleural surface to the cut end of the

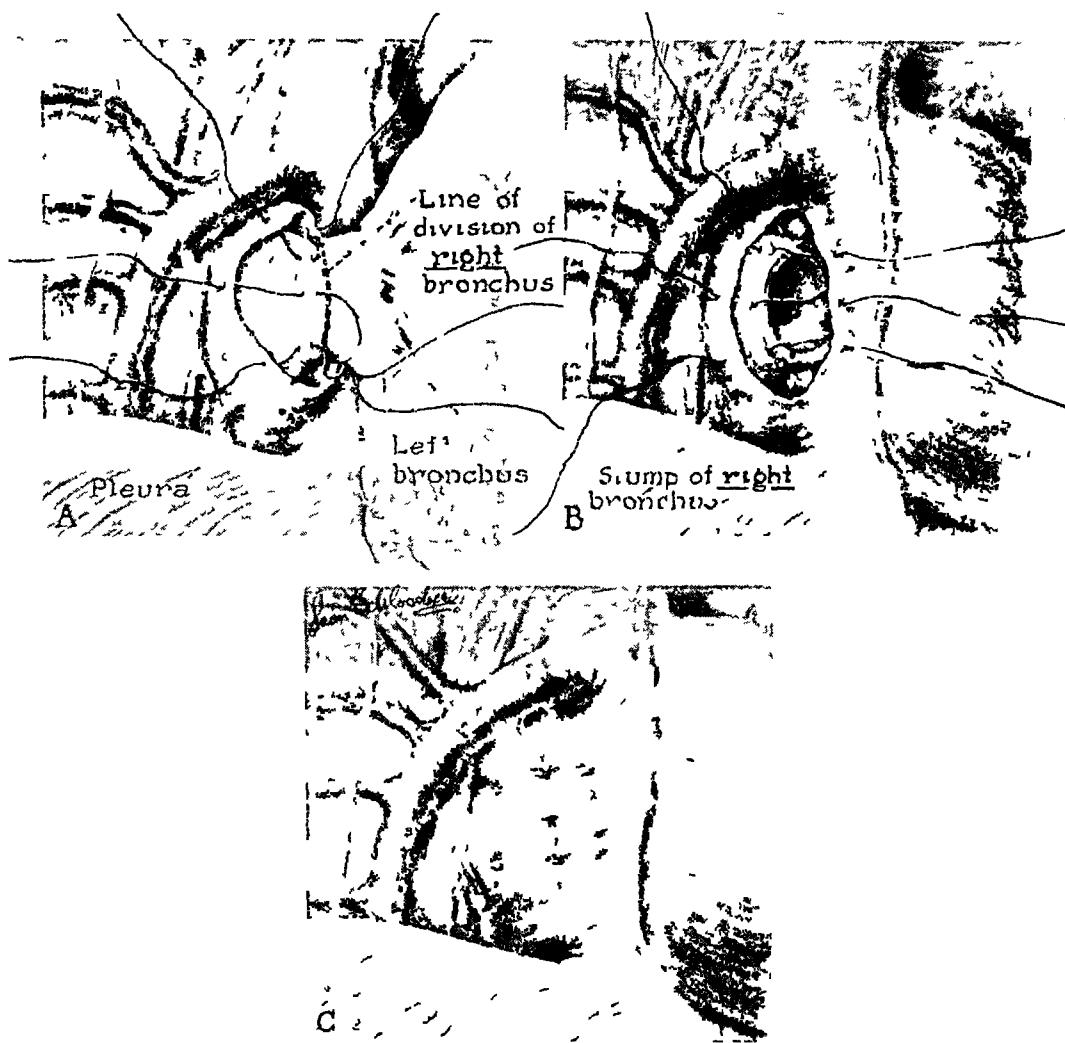


FIG 18—Method of closure of mediastinal pleura over open cut end of bronchial stump

bronchus, the stitches which brought together the incised lips of the mediastinal pleura should at the same time include the slightest bit of the peribronchial connective tissue, situated proximal to the cut end of the bronchus. It is to be noted here that the film-like character of the dog's mediastinum, which is nothing but a simple pleural membrane, allows in proportion a great deal more expansion of the remaining lung, and, therefore, a stronger apposition of its mediastinal pleura to the cut end of the bronchus than would occur in the human being. It would, therefore, seem more important in the human being to secure this approximation of these two structures by sutures.

The manner in which the bronchi healed, as determined by gross inspection, was attended by the formation of less scar tissue, except about the end of the tube, than in the sutured bronchi. The mediastinal pleura as seen from the inside of the thoracic cavity was everywhere smooth and glistening.

Serial sections were made of the amputated bronchial stumps at different

CLOSURE OF BRONCHUS

stages in the healing process, and showed that in the first few days the mechanism of healing was very similar, but that the end-results varied somewhat in their gross and microscopic appearance

The bronchial stump of the animal sacrificed after 24 hours appeared, grossly, to be plugged with an inverted mushroom-shaped clot, resembling in many respects an hematoma (Fig 19) This coagulated mass of tissue

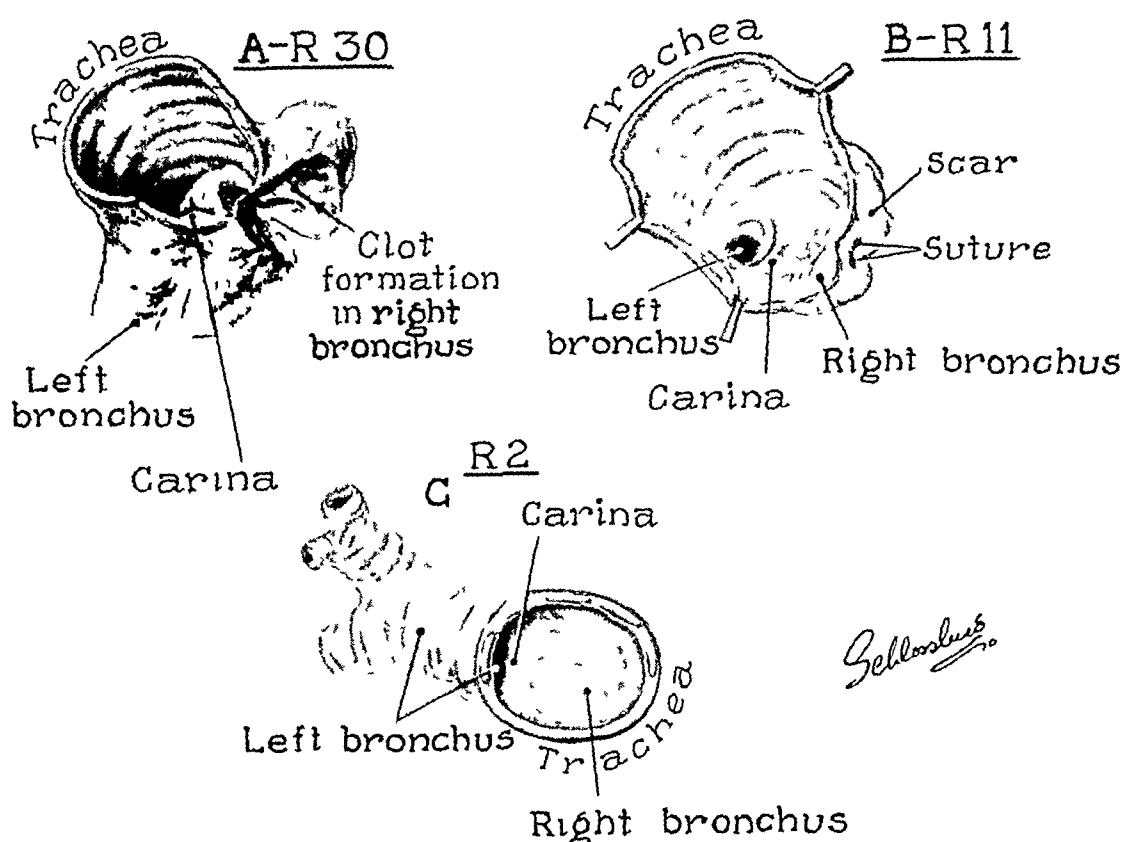


FIG 19—Type of healing observed in gross specimens of second series, in which no sutures were used to close the amputated bronchial stump. A R 30, sacrificed 120 hours after operation, reveals fibrinous coagulated clot protruding into open right bronchus. Cross section of clot formation revealed. As this contracts, it is plain to see from this specimen why, and how, the centermost portion forms an elevated ridge with two lateral depressions as seen in B and C, both of which are healed bronchi in dogs sacrificed after more than four weeks. The suture in B, Dog R 11, was in the pleura, in C, Dog R 2, the elevated ridge has been contracted down by the fibrous tissue substitution, whereas in A, Dog R 30, this substitution has not yet taken place and, therefore, the fibrous clot protrudes further into the bronchus than it will eventually

invariably protruded into the open end of the amputated bronchus, completely filling it, extending into the lumen for varying distances toward the trachea, it covered over the cut ends of the bronchus and blended with the peribronchial and subpleural connective tissue. At this stage, the lumen of the open end of the bronchial stump was always reduced somewhat in diameter and in some instances appeared conical in shape, in others more cylindrical. The microscopic sections corroborated the gross appearance, and showed the open cut end filled with a fibrinous coagulated mass which completely embraced the cut end of the bronchus (Fig 20). Although the bronchus, like a blood vessel, when cut across attempts to close itself, the open end of the tube was reduced in diameter and appeared to be drawn into a cone-shape by contraction of the fibrinous plug. The fibrinous coagulated mass varied in

size, depending on the size of the open end of the bronchus. Microscopically, it consisted of coagulated fibrin in the meshes of which were many polymorphonuclear leukocytes, small lymphocytes, and red blood cells.

Further study showed that as one proceeded from the innermost protruding portion of the fibrous plug peripherally to the overlying pleura the

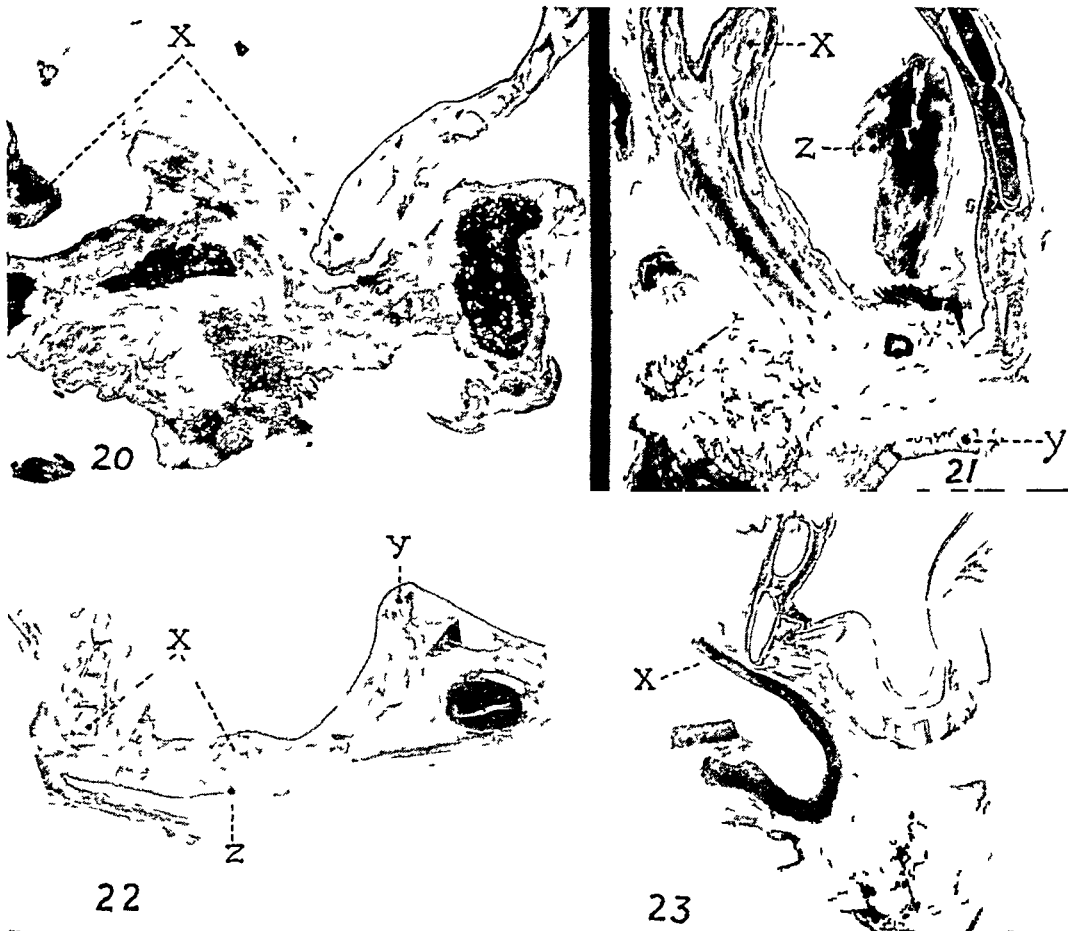


FIG 20—Dog N (8 micra, $\times 4$) Dog sacrificed after 48 hours. Note ends of bronchus at N in which the entire opening is plugged by a mushroom shaped coagulated mass. Red blood cells shown as dark areas in meshes of fibrin. Ends of bronchus embraced by coagulated mass.

FIG 21—R 30 (8 micra $\times 5$) Photomicrograph of gross specimen shown in Fig 19. A Note coagulated mass protruding in bronchus plugging the open end, Z. Carina of trachea is shown at X, mediastinal pleura at Y. This represents the healing of the bronchus at 120 hours.

FIG 22—Dog R 29 (8 micra $\times 6$) Dog sacrificed after two weeks. Left bronchus shows contracting mass of granulation tissue with remaining coagulated fibrous clot still protruding into bronchus. Fibrous tissue has grown into this mass from peribronchial and submucosal tissue. Mediastinal pleura shown at N, carina at Y, and ends of bronchus at Z.

FIG 23—Dog R 18 (8 micra, $\times 4\frac{1}{2}$) Dog sacrificed after four weeks. Although no sutures were used in the closure of this bronchus intubated cartilaginous rings at the cut end of the stump have been drawn completely across the lumen of the bronchus into apposition with each other by the contracting fibrous tissue formed about this open end. Mediastinal pleura shown at X.

microscopic appearance changed. The innermost portion was predominantly coagulated fibrin, the cellular infiltration increasing as the base of the clot was approached. Further, the fibrous mass seemed to blend with the peribronchial submucous connective tissue, as well as with the overlying subpleural areolar tissue. Often hypertrophic lymph follicles, with conspicuous

germinal centers, made up part of this tissue mass. The entire mass was covered over with the mediastinal pleura. As if to emphasize the pull or contraction of the coagulated fibrin, the epithelial lining and submucosa of the cut end would often be drawn in towards the center of the lumen. In the specimens obtained from animals after 96 and 120 hours the fibrinous plug seemed to contract more and become more dense (Figs 19 and 20). The extrabronchial base of the plug was beginning to be invaded by granulation tissue, preceded by invading fibroblasts and endothelial cells. This granulation tissue came from several sources, namely, the peribronchial connective tissue, that lying beneath the mucosa, and also the subpleural areolar tissue (Fig 22). The cellular infiltration seemed to diminish and the fibrinous plug

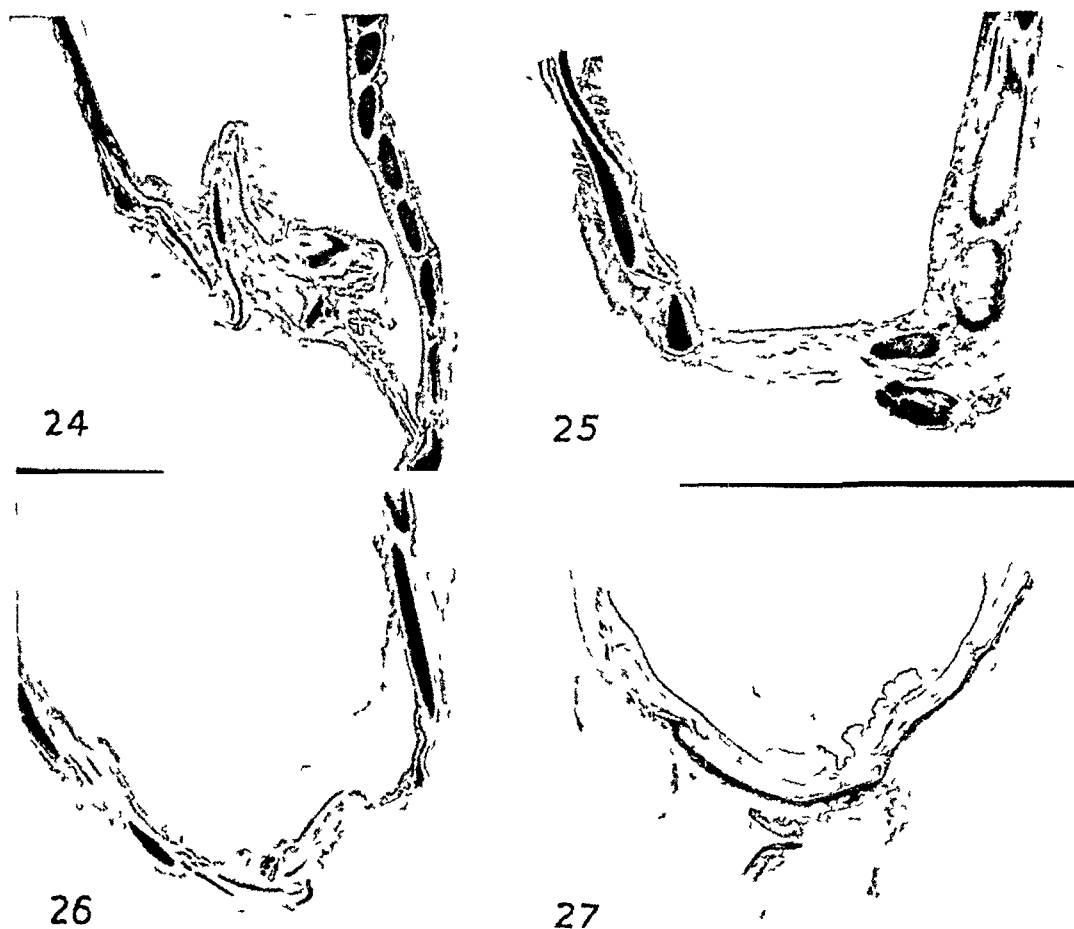


FIG 24—Dog R 5, (micro 8, $\times 4\frac{1}{2}$) Dog sacrificed after four weeks. Although no sutures employed to close open end of amputated stump, contracting fibrous tissue has not only drawn the walls of the cut end of the bronchus together, but actually inverted them. Epithelium has grown over this papillomatous infolding. This type of healing explains the irregular internal surface of these stumps and why there is a central ridge with two lateral recesses as one looks down the inside of the bronchus.

FIG 25—Dog R 6 (micro 8, $\times 6$) Dog sacrificed after four weeks. Cut end of bronchial stump healed over by thin membrane derived from bronchial and subpleural connective tissue. Cut cartilaginous rings have been angulated by the contraction of the fibrous tissue.

FIG 26—Dog R 1 (micro 8, $\times 6$) Healed stump of bronchus by thin membrane derived from peribronchial and subpleural fibrous tissue, slight tapering of cut cartilaginous rings in end of stump. No atrophy of this terminal cartilage.

FIG 27—Dog R 19 (micro 8, $\times 6$) Dog sacrificed after four weeks. Right bronchus, terminal cartilage pulled completely across open end of bronchus. Although no sutures whatever used in the closure, these cartilages were pulled into this position by contracting fibrous tissue. The remains of the coagulated fibrinous clot may be seen in the papillomatous fibrous mass still protruding into the upper blind end of the healed stump.

protruding into the bronchial lumen had begun to retract. The granulation tissue contributed by the peribronchial connective tissue appeared to sweep around the cut ends of the cartilaginous rings, joining with that contributed by the submucosal layer and eventually connecting with the granulation tissue in the center of the lumen or the fibrinous plug. The central portion seemed to spring largely from the subpleural areolar tissue. In some specimens, at the end of 96 hours, the pull resulting from the gradual condensation and contraction of this granulation tissue would not only approximate the cut ends of the bronchus (Fig 23), but in some these edges were actually inverted into the bronchial lumen (Fig 24). In others there was only slight angulation of the cut ends of the bronchus, the granulation tissue forming just a thin occluding membrane across the cylindrical end of the tube (Figs 25 and 26). There were all variations between these extremes. Complete regeneration of the columnar bronchial epithelium and the underlying mucous glands did not occur. Thus, the amount of regeneration in proportion to the internal lining epithelium varied in individual animals. Bronchial epithelium is fairly prolific and the early 72- to 120-hour specimens, as well as those some months old, demonstrated the way in which a thin sheet would grow into all the irregularities and crevices on the internal surface of the protruding, contracted granulation tissue plug. In cross-section, both gross and microscopic, the internal surface was often irregular due to papilloma-like infoldings or bands or both, apparent on the healed inside surface of the bronchial stump (Fig 27). There was never any evidence of regeneration of cartilage. In those instances in which the bronchial walls were approximated by the pull and contraction of the granulation tissue, the cut ends of the cartilaginous ring were, as stated above, either in apposition or infolded or again just slightly angulated. After a few months the specimens revealed that these bits of cartilage became atrophic, staining a slight pink with eosin, and forming part and parcel of the fibrous tissue plug that closed off the end of the bronchus. Microscopic sections of the specimens of the completely healed bronchial stumps, examined some months after the original operation, showed a further progression of the healing processes described. The vascular granulation tissue was transformed into white fibrous connective tissue so that the hitherto coagulated fibrinous plug passed through the stage of granulation tissue to fibrous connective tissue. The final form of the closed or healed stump was pleomorphic, varying somewhat in each animal.

Discussion of the Experimental Results—In the first series of experimental animals it was shown definitely that only in a small percentage of instances had the amputated bronchus healed as sewed at the time of operation. In the largest percentage the healing of the bronchus showed variation in healing, part might be healed as sewed at operation, while the remainder would be wide open and healed over by either a fibrous tissue plug protruding up into the open end of the bronchus, or a fibrous tissue sheet which apparently developed mainly from the nonserous surface of the mediastinal pleura. Regardless of the method in which stitches were placed, whether as inter-

rupted or interrupted mattress sutures, a high percentage of these would cut through the bronchial wall and allow the walls of the cut end of the primary bronchus to separate, either in part or throughout the entire width of the bronchus. The healing would then take place by the sealing off of the open end due to an overgrowth of fibrous tissue from the peribronchial and non-serous surface of the mediastinal pleura. If the latter structure was sewed over the end of the bronchus at the time of operation, complete healing occurred in the manner described in the first series of animals in which mattress sutures were employed. If, on the other hand, as demonstrated in a number of previous series, the mediastinal pleura was not sutured over the end of the bronchus, a certain percentage would leak, regardless of the type of suture or the manner of its insertion, and as is well known, if the bronchus does open between the first and second week, the result is usually fatal in experimental animals.

From this second series of 48 dogs, it may be concluded that the bronchi have healed as completely as those in which sutures were used. There were no infected stitch abscesses in the proximity of the healing cut ends of the bronchi that might eventually have caused a more extensive suppuration, hence, in this respect the tissue repair was more perfect in this series than when sutures were used. Furthermore, the morphologic and microscopic appearance of the healed bronchial stumps presented the same degree of variation observed when sutures were used to close the bronchi. It would seem that the tissue which brought about the final closure of the open end of the bronchus must be considered as being derived mainly from the bronchial walls.

As has been pointed out, the manner in which this closure takes place varies widely. One extreme, in which the cut ends or walls of the bronchus are mechanically pulled, so to speak, towards the middle of the lumen by contracting scar tissue, results in an inturned or even inverted cuff. In this type the healing by granulation is minimal and the original bronchial walls have actually occluded the open end. Thus the tissues bringing about occlusion of the bronchus are almost entirely derived from the bronchial walls. In those instances in which the open end is closed by granulation tissue alone, it is fully apparent in the microscopic sections that the fibrous tissue is derived, at least largely, if not principally, from the peribronchial connective tissue, as well as from the submucosa. A definite contribution from the subpleural areolar tissue is added. Epithelial lining grows in from the bronchial epithelium, but there is no apparent new growth of cartilage. In this latter type of healing it is obvious, therefore, that the bronchial walls also contribute largely to the formation of the tissues which occlude the open end of the bronchus.

It may be stated definitely that in the second series of 48 experimental pneumonectomies, healing of the bronchus took place entirely at the cut end, as no sutures were employed. It may also be said and quite as definitely that in the first series of 36 animals in which the bronchus was closed by inter-

rupted mattress sutures, the healing in the great majority, namely, 82 per cent, of the animals occurred at the open cut end of the bronchus and not along the suture line. It would, therefore, seem reasonable to conclude from our experimental observations that the vital point of healing of the amputated bronchial stump is at the cut end and is not related, in the majority of instances, to the use of occluding sutures.

REVIEW OF THE LITERATURE

The earliest experimental work on resection of the lungs was reported by Gluck,¹ in 1881, when he removed the entire lung on one side from six dogs and 14 rabbits. With the exception of two rabbits, all died in from seven to ten days. In some of the rabbits pericarditis and septic pleuritis developed between the 7th and the 10th postoperative day. The operations were performed with aseptic precautions. It would seem likely that some infection from within as well as from probable opening of the bronchus was responsible for the death of Gluck's animals.

Block² also performed experiments in 1881, with equally discouraging results. He extirpated the lung in five rabbits and four dogs. In only one instance was he able to keep an animal alive more than 14 days. The rabbits died, for the most part, immediately after operation. The dogs lived longer, some even to the 14th day. Unquestionably, sepsis was the cause of death in the animals which did not die from the operation. Four animals subjected to operation one month after the original experiments died of fibrinous hemorrhagic pleuritis.

Biondi,³ in 1884, reported his results, which were the best of those of the early experimenters. An attempt was made to produce a localized pulmonary tuberculosis by means of the injection of tubercle bacilli into the lung. About 25 to 30 days after the initial injection of tubercle bacilli the animals were operated upon and the lung was resected. The experimental animals consisted of five dogs, six cats, and ten rabbits. About half the total number died of septic pleuritis or pericarditis after the initial injection. Four animals died immediately after extirpation of the lung, with seven surviving. In nine animals pleuritis developed following extirpation of the lung.

Willard,⁴ in 1891, performed a successful pneumonectomy in a dog by suturing the stump, which he ligated *en masse* into the wound. In 1889 Murphy⁵ lost eight of nine dogs with septic pleuritis. In 1907, Tiegel,⁶ and Mitt,⁶ advocated the use of a loose silk ligature placed about the hilum, to be followed by peripheral ligation of the vessels to that portion of the lung to be resected. The bronchial stump was cauterized and ligated distal to the first mass ligature. This method, as would be expected, was followed by hemorrhage and bronchial fistula. Frederick,⁷ in 1908, advocated separate ligation of the hilar structures and removal of the mucous membrane from the bronchus to such an extent that the denuded bronchial wall could be approximated and ligated.

Danielson,⁸ in 1908, suggested the use of silk to close the main bronchus

Robinson,⁹ also in 1908, performed thoracotomy upon 30 dogs under positive pressure anesthesia. In 12 of the animals pleurotomy was performed without interference with the lung. In 15 animals operated upon, part of or an entire lobe was resected, one with removal of two entire lobes and one with removal of the entire lung. There were five deaths from sepsis, one case of sepsis being due to leakage from the bronchial stump. There were four additional cases of infection, due to localized empyema or parietal wound infection, the animals, however, recovered.

In 1909, Halsted¹⁰ performed 21 consecutive thoracotomies in which there was only one primary infection of the thoracic cavity. These results contrasted strikingly with the earlier results, marking what might be called the advent of aseptic surgery applied to the thorax. Halsted, assisted by Willis D. Gatch, concerned himself chiefly with the bronchi and the vessels at the root of the lungs and various lobes. Occlusion of the main, and of the primary and secondary divisions of the bronchus was practiced, various methods and almost all degrees of occlusion being tested. The lung was only occasionally excised. Bronchial occlusion was secured by ligations with metal bands. In no instance were the experimenters able to crush the bronchial wall with the encircling bands, and in no instance did these bands give rise to pulmonary emphysema or dilatation of the bronchus. The bronchus could not be obliterated by bands. They also found that ligatures of black silk did not completely occlude the bronchus or permanently obliterate it unless the mucosa was crushed. Permanent obliteration was accomplished following bisection of the bronchus, careful excision with the scalpel of its mucosa, and approximation of the raw surfaces by running sutures of fine black silk. By this method the bronchus could be converted into a solid fibrous cord. Halsted gave up the inversion of the bronchus because it seemed too short for nice adjustment.

In this article Halsted did not refer to the use of mattress sutures nor did he state whether the sutures were put in the end of the bronchus or through the bronchial wall proximal to the cut end. We have repeated his observations, employing mattress sutures, and have found the closure to be very satisfactory in the dog and also in the human being. Halsted's experiments represent, up to that time, the most fundamental contribution to the surgery of the lung, particularly with regard to the closure of the primary bronchus.

Willy Meyer,¹¹ in 1909, described an inversion method in which the bronchial mucosa was undisturbed. In 21 extirpations there were four deaths due to sepsis and to leakage from the bronchial stump. The main bronchus was crushed and ligated. The method of Willy Meyer is undoubtedly a very satisfactory one for experimental pneumonectomy, although unnecessary in the light of our present experience, but this method is a typical example of one described many times since in the literature, which is totally inapplicable to human beings, mainly because of the stiffness and rigidity of the bronchi.

Robinson and Sauerbruch,¹² in 1909 reported 38 total extirpations of

the lung in which there were four recoveries. Their report of other experimental results included those of von Haecker. They claimed that five animals died from sepsis and 11 from leakage from the bronchial stump, and that in 18 there was a transudation into the pleural cavity upon the operated side, followed by death. This was more than likely a septic pleuritis.

Quinby and Morse,¹³ in 1911, in their series of experiments, pointed out, for the first time, the importance of peribronchial tissue and its use in the closure of the bronchus, and called attention to the fact that they were never able to secure an air-tight closure of a bronchus which had been thoroughly isolated before tying. They further suggested, in accordance with the point brought out by Tiegel, that bronchial wounds heal best when the stitches are placed only in the peribronchial tissues. They also stated that inversion of the primary bronchus on the right side, before the departure of the branch to the upper lobe, is impossible because it is too short. Quinby and Morse called attention, for the first time, to the advantage of employing a lappet of lung which is opposed by a stitch to the hilus denuded of pleura because as they said, "as is well known the lung has adhesive and walling-off power quite like the omentum," and they recalled the adhesions of the lung to an esophageal suture in previous experimental work. They also described, completely, the intrathoracic restitutional mechanism by which, following total pneumonectomy, the vacant thoracic cavity is filled up by the heart and the contralateral lung moving over toward the operated side. "The diaphragm rises and the ribs flatten with their interspaces shortened." Overinflation of the lung as the thoracic cavity is closed was recommended. Another valuable suggestion that these authors made is painting with tincture of iodine the region of the lung root after it has been carefully dried and the toilet of the wound completed. This is the first time this important step had been mentioned.

Quinby and Morse operated upon 38 dogs, 30 of which recovered and eight died. The right lung was excised in 17, with three deaths, the left in 21, with five deaths. There was no mortality in the last nine cases. Unquestionably, Quinby and Morse's contributions to thoracic surgery must be considered among the most fundamental, and would seem to have been insufficiently emphasized in the literature.

In 1912 Garré¹⁴ advocated sewing a piece of lung tissue over the open bronchus after having placed a ligature about the latter structure. This method has been suggested independently, in recent years, by Churchill.

Henschen,¹⁵ in 1914, proposed the introduction of a roll or plug of fascia into the lumen of the divided bronchus, the stump being closed over it. This procedure was later carried out by Halsted and Ciowe. Giertz,¹⁶ also in 1914, used fascia to close the bronchial stump by suturing it over the end of the bronchus and using silk stitches to hold the fascia in place. The bronchus was first closed with mattress sutures of silk and then covered by the fascia which was sutured to the peribronchial tissue. This method was similar to but not exactly like the one advocated more recently by Taffel in 1940.

Giertz operated upon 10 dogs and lost two of them. In 1914, Kawamura¹⁷ reported his observations on experimental pneumonectomy, having operated upon 23 animals, three died of sepsis, two deaths being secondary to leakage from the bronchial stump.

Heuer and Dunn,¹⁸ in 1920, reported their results on experimental pneumonectomy in which they employed all the different methods of suturing the bronchus that had been used before that time. Their results confirmed many of the previous observations made by Quinby, and also by Kawamura, in regard to the fate of the intrapleural cavity resulting after removal of the lung and the methods for its obliteration, as well as the reactions on the part of the remaining lung to the presence of simple dilatation of the definitive respiratory unit, namely, the ductus alveolaris, the atria, and the alveoli, instead of an hypertrophy and hyperplasia of the lung parenchyma. In 23 dogs in which total pneumonectomy was practiced there were 13 recoveries and 10 deaths, the fatalities occurring from four days to two months after operation. Six of the deaths were due to epidemics of distemper. The post-mortem examinations in this group did not show a single instance of infection of the parietal wound or pleura or leakage from the bronchial stump. One animal died of a simple pneumonia, unassociated with other evidences of distemper. One animal died from starvation two months after operation. Two animals died of acute pneumothorax, the result of leakage from the bronchial stump, and in one of these the failure to secure adequate closure of the bronchial stump was intentional. One died of necrosis of the bronchial wall following application of a flattened metal band. In eight animals the bronchus was crushed and transfixed by a single ligature of heavy EE silk, and it is stated that in none of these animals did the bronchial stump leak, nor was there any pleural infection, all having lived more than one month following operation. The size and age of the dogs so operated upon was not stated. This point is brought up because it is a well known fact that in younger dogs and puppies, as well as in children, simple ligature is often efficacious, whereas it is not so in older and larger dogs and in adult human beings. It is also interesting to note that in five of the dogs, so operated upon by Heuer and Dunn, the bronchial stump had retracted into the mediastinum and was covered by mediastinal pleura, although this had not been sewed over the stump at the time of operation.

It is interesting to note that the illustrations of the healing of the bronchus, in the gross, show that exactly the same type of healing occurred in the bronchi which were ligated that we, in our series, found to occur in the end of the bronchi in which no ligature or stitches were placed, the mediastinal pleura having been merely drawn over the open end. I refer particularly to Figs 4 and 5 in Heuer and Dunn's article. This fact would seem to suggest that, in their series, the ligated bronchi had become spontaneously covered with mediastinal pleura and had healed as did those in our series that were intentionally covered with serous membrane the ligature probably having cut through and allowed the walls of the bronchus to open.

up, as shown in their illustrations. If the ligation had held, the bronchial stump should have remained conical as left at operation. In illustration 3A, however, the end of the healed bronchus is of the same diameter as the lumen of the proximal portion of the stump. Figure 3A, especially, looks as if the walls of the bronchus had completely opened and subsequently healed by a fibrinous plug in the cut end.

The microscopic sections are even more suggestive of healing in the manner of those of our second series, in which no stitches were placed in the wall of the bronchus. In their Figure 6 the mesial section is again similar to our experiments in which no attempt was made to close the bronchus. In other words, the bronchial stump is healed with a fibrous plug, and if a conclusion can be reached from the study of photographs, it would seem likely that a number of bronchi in Heuer and Dunn's series had opened by being cut through by their ligatures or sutures and had healed in the manner described in our second series. Their illustrations, both gross and microscopic showing the methods of healing following the use of different types of ligatures and sutures in closing the bronchus, are exactly similar to our illustrations in which the bronchus healed without any sutures or ligatures.

As one reviews the sections of the healing of the bronchial stump in the article by Heuer and Dunn, it would seem probable that their excellent results were obtained, as were ours, by healing of the bronchus through a fibrous or fibrinous granulation plug rather than from apposition of the walls by any particular method of suture.

We are particularly interested in Heuer and Dunn's report because in our first series of animals we also were of the opinion that the method of suture employed had a great deal to do with the type of healing. We soon discovered, however, from the gross and microscopic appearance of the healed bronchial stumps, that our results were exactly similar in every respect to those of Heuer and Dunn, and, except for the fact that they intentionally employed for closure two methods which they were sure would end fatally, their results were as favorable as ours. Heuer was the first to demonstrate the microscopic appearance of healed bronchial stumps and also to point out that similar results were obtained following a variety of methods of closure.

In 1924, Bettman¹⁹ reported his experiment in which he performed lobectomy, pneumonectomy, and isolation of the entire lung in dogs. He stated at the beginning of his paper "After a protracted study of the subject and after numerous experiments, it must be admitted that we have not been able to close the large bronchi with any certainty of success by any of the methods reported. We have arrived at conclusions diametrically opposed to those of Heuer. According to our experiments, an isolated large bronchus will not heal. Smaller bronchi can be sealed, but the tissues which close them are not derived from the bronchi themselves, but from the peribronchial structures. In short, following pneumonectomy, our dogs almost inva-

riably (there were two exceptions) died. Following simple lobectomy the dogs almost always lived. In the group in which lobectomy was done the secondary bronchus of the lobe was closed with a simple ligature of No. 2 catgut, and, at autopsy, it was found that the visceral pleura of the adjacent lobes was glued over the amputated bronchial stump by adhesions. On microscopic examination the sections showing the healed bronchi revealed that the occluded end was blunt rather than conical. This indicated to us that the ligature had given way and the bronchus, opened up, subsequently, healing, as in our series, in juxtaposition to the pleura. Bettman states: "In the majority of our sections the remaining lung was plastered over the cut end of the bronchus and it was apparently this reaction which had saved the bronchus from reopening. The fibrous tissue which had closed the bronchus seems to have sprung from the visceral pleura firmly holding this pleural cap over the cut end."

Bettman's illustrations, both camera lucida diagrams and photomicrographs, are similar in every respect to ours. He mentions cysts lined with epithelium which appeared in the blunt occluded end distal to the closure of the lumen of the secondary and tertiary bronchi. These cysts were assumed by Bettman to be due to infolding of portions of the lumen of the bronchus by the ligature, but he thought that these cysts reduced the strength of the occlusion of the bronchus. This has been found by us not to be true. The cysts, as we have pointed out, are due entirely to the preservation of live epithelium distal to the ligature or suture line of the bronchus regardless of whether it is a primary, a secondary, or a tertiary bronchus. Also, we feel that Bettman considered the bronchial wall inert. We agree with this observation from the standpoint of regeneration of cartilage, but in no other respect. The peribronchial connective tissue together with bronchial smooth muscle, muscularis mucosae, and the fibrous tissue springing therefrom, as well as the mucosa, contributes always to the closure of the end of the bronchus. In one instance Bettman mentions a lobectomy of the right lung in which the bronchus was ligated and on healing

"there was a very fine membrane of connective tissue which stretched across the bronchus much as a thin piece of rubber might be stretched over the end of a metal tube. Any slight increase in pressure undoubtedly would have torn open the bronchus." This assumption, of course, was found by our differential pressure readings to be far from the actual case. This thin membrane of connective tissue which Bettman refers to is an ideal form of healing in closure of the bronchus.

In Bettman's series of 26 dogs, in which the *total lung* had been removed all except one died within the first week. After reviewing Bettman's experiments, the only explanation that we can make is that in those in which catgut was used as the suture material, the catgut probably gave way. Cauterization of the stump of the bronchus and crushing it probably also played their part because autopsy revealed that the stumps whether inverted by silk or by catgut, opened. This result must have been due to necrosis of the tissue in

which the stitch was taken as a result of crushing and cauterization. If we may interpret experiments from a previous author's work, it would be our opinion that if these stumps, in spite of the fact that they were crushed and cauterized, had been covered with mediastinal pleura or pleuralized, in all probability, a high percentage of them would have successfully healed and the dogs would have survived.

It would seem to us that Bettman's series is sufficient evidence that catgut should not be used, and also that any trauma, such as thermal or chemical cauterization or mechanical crushing, should be carefully avoided.

In a later contribution Bettman, *et al*,²¹ in 1928, reported another experiment which supported the impression that we obtained from Bettman's first report, namely, that necrosis of the cut end of the bronchial stump and the tissues surrounding it will prevent primary healing of the bronchus and thus allow ligatures in this region either to cut through or to pull out. Such necrosis will also prevent successful *per primam* agglutination of the amputated bronchial stump to opposing structures such as overlying pleura. Their reports show that in a series of six dogs, in which there was massive ligation and crushing of the stump previous to the lobectomy (not pneumonectomy), four of the animals died of reopening of the bronchial stump, whereas in seven dogs in which the vessels were individually ligated, without trauma from crushing or cauterization, only one died from some cause other than opening of the bronchial wound. These observers performed only one total pneumonectomy and the method of closure of the bronchus was not given, but it is to be assumed from their report that it was probably ligated with catgut. This dog died on the 6th day from reopening of the bronchus, and the authors came to this conclusion: "We did not feel justified in sacrificing any more animals to prove that the bronchial stump fails to remain closed following pneumonectomy in contradistinction to lobectomies."

It is unfortunate that Bettman and his coworkers did not apply their lobectomy technic to pneumonectomy, in other words, that they did not cover the amputated bronchial stump, for their observations in the healing of the secondary and tertiary bronchi following lobectomy are similar in all respects to our observations following total pneumonectomy.

Feiermann,²⁰ in 1925, reviewed various methods of closing the bronchial stump, and concluded that the method to be preferred was that suggested by Willy Meyer. Up to that time, however, previous authors had had just as successful healing with other methods of closure as with that advocated by Meyer.

Joannides,²² in 1928, suggested leaving a portion of the lung tissue or a lobe in contact with the amputated bronchial stump, in other words, cutting through a portion of lung tissue. This procedure is impractical and obviously would prevent one from doing a total pneumonectomy. It is, therefore, an argument that, in our opinion, is not pertinent.

Schleuter and Weidlein,²³ in 1928, suggested invagination of the bronchus by cutting the primary and secondary bronchi between ligatures and then

inverting each with a purse-string suture of No 1 chromic catgut and, in the case of the primary bronchus, reinforcing it by three mattress sutures of silk. By this method the author performed four total pneumonectomies, following which one animal died of empyema on the fourth day. The objection to this method is the same as to the method of Willy Meyer, in that it is not practical and applicable to the human being, nor is it necessary for a successful closure of the primary bronchus in the animal.

Nisson,²⁴ in 1931, suggested ligation *en masse* as a two-stage procedure, surrounding the lobe to be excised with a coarse silk-mesh bag to obliterate the pleural cavity, followed by amputation two to four weeks later. This method may have some application in suppurative cases, but would, it seems to us, prove inefficacious when dealing with malignancy.

Adams,²⁵ in 1931, attempted to produce bronchial stenosis by the use of 35 per cent silver nitrate injected intrabronchially prior to operation. This procedure would seem ideal but was not successful in our hands, except in one case in the human being in which there was a small opening in the bronchus following amputation of the lung. This method of Adams' was successfully used in experimental closure, but we believe that the human bronchus is too rigid to be stenosed in this manner.

In animal experimentation Blalock,²⁶ in 1933, found the method of Adams to be associated with a rather high mortality due to inflammatory sequelae following the application of the silver nitrate to the bronchial wall.

Longacrie,²⁷ in 1935, using a method of inversion of the bronchus, operated upon a series of 30 dogs and found, as have others, that silk ligatures were to be preferred to catgut; he showed that in Series (A), 12 dogs, in which chromic catgut was used, the mortality was 75 per cent, and the incidence of bronchial fistula 66.6 per cent, whereas in Series (B), 18 dogs, the mortality was 16.6 per cent, and the incidence of bronchial fistula 5.5 per cent, where the suture material employed was fine and medium silk.

It is interesting that in the experiments of Longacrie,²⁷ in 1935, in which catgut was employed and the bronchus opened, he found the healed closure to be the same as in our series in which no sutures were placed in the cut end of the stump. He says "The openings were sealed over with a loose network of newly formed granulation tissue. By the end of three or four weeks this had become more dense and the stump consequently more solid. By this time the external surface of the stump was pleuralized and the mucous membrane was starting to cover the inner surface of the bronchial stump."

It is interesting to note that Figure 9, in Longacrie's report, showing the healing of the bronchial stumps demonstrated, as did Heuer's and ours, the same type of healing, yet the method of closure employed by Longacrie was entirely different from those used by Heuer, and by us.

In 1937, Thomas *et al*,²⁸ presented a technic for total pneumonectomy in animals in which they stated that two encircling sutures were placed about the lumen of the bronchus tight enough to occlude the lumen, but not tight enough to crush the bronchus or the peribronchial tissue. This procedure requires a

delicacy in tying which is not given to the average surgeon for the resistance of the epithelium to the occluding ligature must be very difficult to appreciate. Peribronchial tissue was utilized by them to oversew the stump of the bronchus. In all three layers of suture line were generally used, and the bronchial stump was pleuralized, much as the cervical stump is peritonealized following hysterectomy. Under "*Results*" they did not mention the number of dogs operated upon, but merely said that a "few" were lost. Under "*Cause of Death*" they stated that "for the few dogs that died after operation the average length of life was 7.3 days." They did not state how many dogs died. No mention is made of the method or type of healing as evidently the bronchial stumps were not examined postoperatively.

In 1940, Taffel²⁹ suggested closing the opening in the lower end of the trachea, following removal of the left primary bronchus "with a stamp of deep thoracic fascia." He employed this method successfully in two dogs. The description of the microscopic findings and the illustrations of the healed bronchial stump (Fig. 10, Dog No. 426) again shows the same type of healing that we found to take place in our second series. The fascial grafts which Taffel used had disappeared after 8 and 12 weeks, when the dogs were sacrificed. As Taffel suggests "The graft did not appear to remain viable but acted as a temporary and a tight scaffold." As in our series, the bronchus in these two instances was held together by granulation tissue. The cut cartilaginous rings are almost approximated by the pull of the contracting fibrous tissue, as shown in Figure 10 of Taffel's article. Taffel's suggestion is a very ingenious one which will undoubtedly prove to be useful in certain cases of pneumonectomy in man.

Stafford,³⁰ in 1941, reported a plastic closure of the bronchus in a series of 33 dogs, in which three died because of technical difficulties and three from tracheal fistula. Stafford also covered the operative field with mediastinal pleura, simply with the idea of covering over a denuded area. No data or description of the microscopic appearance of the healing of the amputated bronchial stumps are given. However, it is unlikely that such a method, in which flaps of the bronchial wall are to be used in order to close the open end of the amputated bronchus, would be applicable to the human being. Other than the anatomic differences between the primary bronchus of the dog and the human being, that is, the increased rigidity of the human bronchus, there is also the fact that the primary bronchus is usually involved in the growth for which the lung is to be removed. There is therefore, not enough of the bronchial wall remaining from which to select and cut a flap.

Thus it would appear that in the majority of instances of experimental pneumonectomy the bronchial stump healed in the same manner regardless of the type of closure employed, whether sutured or ligated or whether any closure was attempted at all, provided the end of the amputated stump had been pleuralized, either intentionally or spontaneously. This fact would

seem to nullify the influence of any particular type or method of suture upon the manner in which the healing of the bronchial stump occurred

CLINICAL OBSERVATIONS

Clinical observations on the closure of the human primary bronchus in a series of 61 consecutive total pneumonectomies, extending over a period of nine years (since 1933), have emphasized the fact that to obtain the optimal healing of this structure, certain procedures in the closure must be observed. In the early cases of this series various methods were employed to close the bronchial stump, primarily because the clinical data on this subject were extremely meager, and, secondarily, because suggested procedures emanating from experimental pneumonectomy were not applicable to the human being. It was, therefore, concluded that closure of the primary bronchus in the human being was an individual problem due mainly to anatomic differences from other species, which could not be worked out in the laboratory but must be solved in the operating room. Thus, many different methods of closing the human bronchus were resorted to, which employed both absorbable and nonabsorbable suture material applied in various ways. It was early recognized that absorbable sutures were too frequently unreliable and this type of suture was soon given up. Circumferential ligatures of fascia, braided silk, different wires, and bands were discarded because it was found that they would cut through the bronchus. In 1939, the employment of a primary encircling ligature about the bronchus was suggested in addition to the use of mattress sutures to close the end of the stump. Although this method was the most successful employed in this series of cases up to that time, in many instances the closure was unsatisfactory. In four cases the circumferential ligature was coughed up after the patients had been discharged from the hospital for some months. In others, there was reopening of the stump to a greater or less degree. The majority of these patients lived, and fortunately a localized area of suppuration was walled off which drained for months, but eventually healed. In three, it was necessary to perform a posterior thoracoplasty to bring about closure of the chronic empyema cavity and of the bronchus.

The success or failure of the closure depended on unknown factors aiding or interfering with complete healing. Why, with the same technic of closure, would the majority heal solidly while a minority opened to some degree? Of the 61 patients upon whom total pneumonectomy was performed, 47 (77.1 per cent) lived. In 34 of these (72.3 per cent) the bronchus healed without leaking. An opening occurred in 13 (27.7 per cent) who survived and, excepting the three upon whom a posterior thoracoplasty was performed, the bronchial fistula, in all, eventually closed spontaneously. Autopsy on the 14 (22.9 per cent) patients who died in the hospital revealed that in three the bronchus had opened wide within the first week. Two of these closures were made with catgut and were early cases in the series, but one was a recent case closed with silk sutures. This patient's

case was of particular interest and will be discussed later in this paper. Absorbable sutures are no longer employed as they are now considered unsafe. Nevertheless, with the first 30 patients there was increasing apprehension concerning the clinical postoperative course during the second week. It has been usually about the tenth to the fourteenth postoperative day that, beginning with an elevation of temperature and pulse rate, progressive and unmistakable signs of bronchial leakage have occurred in these unfortunate patients. Including the three patients who succumbed as a result of opening of the bronchus, together with the 13 who survived partial opening, that is to say, 16 cases out of a total of 61 complete pneumonectomies, the closure of the primary bronchus was insecure or failed to heal solidly in a startlingly high percentage of cases (26.2 per cent).

At a loss to correct our faults following a critical analysis of all the experimental and clinical data available, we decided to take the problem to the laboratory in order to determine the mechanism by which and the manner in which the bronchus would heal, and at the same time to determine a method which would prove to be satisfactory in the experimental animal and applicable as well to man. The experimental data have been presented in the first part of this paper.

In addition to the experimental observations, however, the opportunity presented itself on six occasions to study the method of healing in the human bronchus from autopsy specimens. Autopsies were obtained on six patients who had survived total pneumonectomy for varying lengths of time and in whom the cause of death was unrelated to the operation. From the clinical standpoint, the bronchi had healed solidly in each case, and this impression was confirmed at autopsy by increasing the intratracheal pressure sufficiently to hyperexpand the opposite lung without producing demonstrable leakage from the closed bronchial stump. As in the experimental animals, the operated side was filled with water in order to facilitate the detection of bronchial leakage by the appearance of bubbles. In each instance the bronchus had healed completely and there was no leakage. When microscopic sections of these healed stumps were examined, however, it was noted that the manner and method of healing varied somewhat in the different individuals but followed exactly along the lines of our experimental observations. In not a single instance had the bronchi healed as sewed at operation, because in each case the ligatures or sutures or both had cut through and had either been coughed up or had remained encysted outside of the bronchial wall. As in the experimental closure the open end of the bronchus had healed by becoming filled with a fibrous tissue plug derived from the peribronchial, submucosal, and subpleural areolar tissue. In one, the walls of the bronchus had actually become inverted by the pull of the contracting granulation tissue. All of the healed stumps were more of the cylindrical than of the conical type. In the first patient death occurred two days after total left pneumonectomy, as a result of a plugging of the mitral orifice by a pedunculated fibromyxoma of the wall of the left auricle. In the



FIG 28—Autopsy CHI (micro 10, $\times 4\frac{1}{2}$) Shows walls of bronchus at X, organizing granulating tissue plug at Y, occluding the bronchus, cutting silk sutures shown at Z, others probably discharged into lumen Specimen two weeks postoperative



FIG 29—Autopsy JHH, No 14428 (micro 10, $\times 4\frac{1}{2}$) Death 19 days postoperative Bronchus originally closed with interrupted mattress sutures Cuff of open end of bronchus inverted by contracting fibrous tissue about the healed end of stump Mediastinal pleura noted at X Contribution of bronchial fibrous tissue observed at the ends of the cartilaginous ring approximating the ends of the bronchial stump

microscopic sections the very early stages of the closure of the bronchial stump by a coagulated fibrinous clot was observed, which corresponded in all respects to our experimental findings. In this patient the bronchus had been closed with interrupted mattress sutures of silk, but the open cut end distal to the suture line was already undergoing the early stages of cicatrization due to the formation of surrounding granulation tissue.

The second patient in this series of autopsies died from a massive pul-



FIG 30—Autopsy J H H No 16923 (micro 10, $\times 5$) Bronchial walls, cut end of bronchus shown at X. Fibrous tissue mass plugging end of bronchus. Patient died one month following operation. Fibrous mass separated from one bronchial wall during cutting of section.

monary embolus 14 days after removal of the entire left lung. The microscopic sections of the bronchial stump (Fig 28) showed the open end filled with granulation tissue over which epithelium had just begun to grow. Silk sutures which had cut through could be seen in the lumen and also outside of the bronchus. The bronchus in this case also had been closed with interrupted mattress sutures of silk, and although there was no clinical evidence of it, the silk sutures had already cut through by the end of two weeks, as demonstrated by the microscopic sections. Nineteen days after the right lung was removed another patient died of pulmonary infarction of the entire left lower lobe. A photomicrograph (Fig 29) showed perfect infolding of the entire cut end of the bronchus. In this instance the amputated stump was also closed with interrupted mattress sutures of silk, leaving an open cuff of bronchus distal to the suture line. No attempt was made to invert the cut end of the bronchus. The silk sutures had cut through, but the open cut end had already healed sufficiently to prevent leakage. Thus, as in the experimental closure, each case seemed to heal in a slightly different manner as to the degree of participation of the bronchial walls by

infolding or invagination. In this instance the bronchial walls had been drawn together and inverted by the contracting granulation tissue so that only a small infolded area remained to be epithelialized. Following a low grade fibrinopurulent pericarditis which developed one month after total left pneumonectomy, the bronchus, although clinically solidly healed, as seen at autopsy, proved, by microscopic section, to have opened up into a cylindrical tube, the cut end of which was filled with a mass of fibrous granulation tissue (Fig 30). Not one of the mattress sutures was in evidence although at least six had been inserted at the time of operation. The fifth patient in this series, who was operated upon in the fall of 1933, when her left lung was removed, returned six months later, and succumbed as a result of cerebral metastases. At the time of operation the bronchus had been closed with interrupted silk sutures near the cut end. The microscopic section is not shown because the original block that included the entire cylindrical healed end was cut across one side only. The remainder of the block was misplaced but part of the fibrous tissue plug could be observed. Only one small wall of the bronchus was included in the section, and although a badly planned section, the method of healing was obvious, that is to say, the open cut end had been sealed with fibrous tissue.

Following the now famous case of Evans Graham, the first pneumonectomy performed in the Johns Hopkins Hospital was undertaken June, 1933, in a child three and a half years of age, for fibrosarcoma of the bronchus. The left primary bronchus was simply tied off with a braided silk ligature. The patient remained well, but unfortunately four and a half years later was drowned. The body was recovered and her father sent the thoracic viscera to us for study. Figure 31 is a photomicrograph of a section of the healed bronchial stump. It is obvious that the bronchus had been completely occluded by a fibrous plug of tissue. The remains of the silk ligature could be found in the fibrous mass of tissue surrounding the healed end.

It seemed, therefore, that the healing process of the primary bronchus in man was similar in every respect to that of the dog, that regardless of the type of sutures or ligatures employed to occlude the bronchus, they would, in the majority of cases, cut through the bronchial wall. If the sutures ulcerated toward the lumen they would be coughed up, but if they migrated towards the periphery they would be buried in the fibrous peribronchial tissue. Likewise, in man, as in the dog, healing of the bronchial stump took place, in the majority of cases, about the cut end of the bronchus some distance peripheral to the occluding suture line. The sutures or ligatures closed the bronchus temporarily, but could not be depended upon to maintain this occlusion for more than a week or ten days, during which time healing would occur at and about the cut end. The tissues that took part in the healing were derived mainly from the bronchial walls.

DISCUSSION—Based not only on experimental evidence, but also on observations on the healing of the primary bronchus in man, as determined

at autopsy, a method of closing the primary bronchus has been planned and employed in this series with far greater success than any used heretofore. In 27 consecutive patients in whom the bronchial stump has been so treated, there have been only two (7.4 per cent) in whom the bronchus opened. It is our opinion that the leakage in these two cases can be explained as due not to the method of closure, but rather to an improper application of the method.

Based on previous clinical experience, together with our experimental

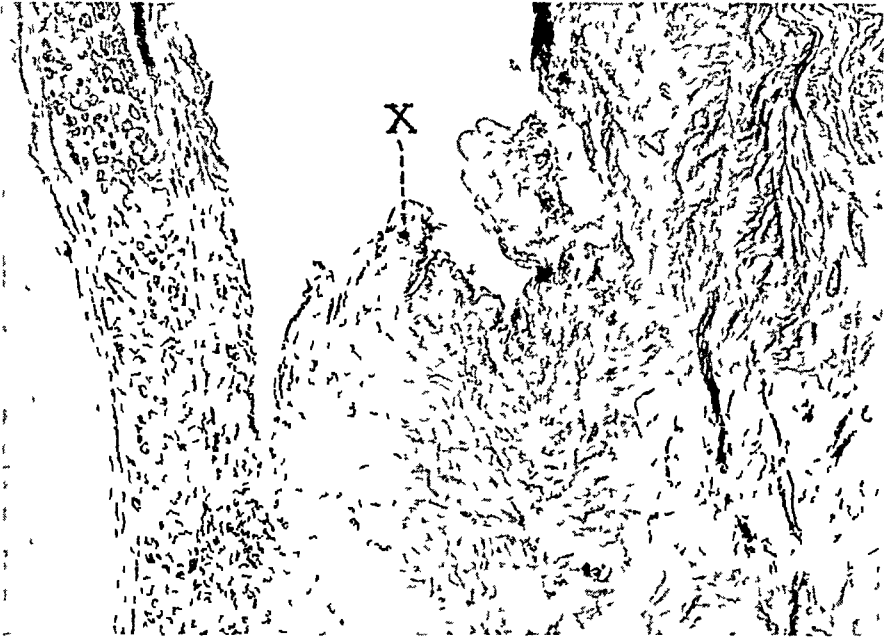


FIG. 31—Autopsy J. H. H., No. 14937 (micra 10 \28). Fibrous tissue plug in end of bronchus completely organized, shown at X, bronchial walls at Y. Death 4½ years after operation, patient drowned.

evidence, the method of closure of the primary bronchus in the human being which we feel offers the greatest opportunity of secure closure, is as follows:

The primary bronchus should be amputated near the bifurcation of the trachea leaving only a short stump, so that this may be contained well within the mediastinum. The amputation should be executed with the scalpel in order that as little damage as possible is done to the cut end of the stump. Crushing or any form of cauterization, either thermal or chemical, should be strictly avoided because devitalized tissue must be sloughed off or replaced by viable fibrous tissue from the neighborhood. This process invites infection, ever present in the human bronchus to a greater or less degree. Also, primary agglutination of the vital amputated stump of the bronchus to the surrounding or overlying areolar tissue thus would be prevented. Another reason why the bronchus should be amputated high and should be disturbed as little as possible in its areolar bed in the mediastinum is in order that the stump may be surrounded by vigorous granulation tissue

CLOSURE OF BRONCHUS

originating from the mediastinal areolar tissue and also from the undisturbed peribronchial tissue. The inferior thyroid artery gives off small branches to the lower end of the trachea and the first part of the primary bronchus. In some individuals the bronchial artery applies itself to the posterior aspect of the primary bronchus some distance from the bifurcation of the trachea, so that there may be a space between the areas supplied by the inferior thyroid

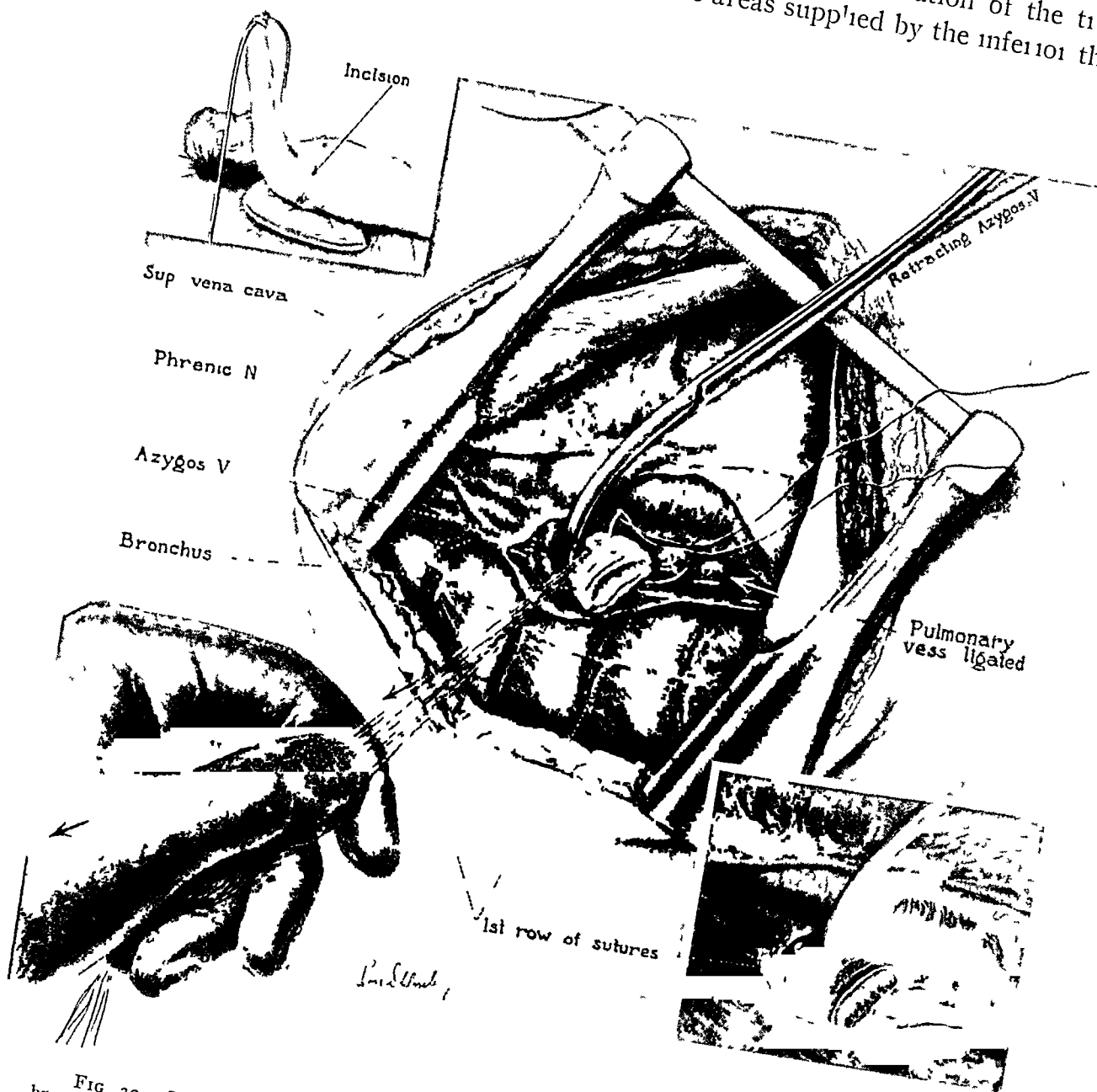


FIG 32—Shows position of patient on table and interolateral incision. Closure of right primary bronchus, mattress sutures leaving viable cuff of bronchus distal to suture line. Insert, lower portion, shows sutured bronchus with viable open cuff residing in mediastinum.

arteries and the bronchial vessels that has a relatively poor circulation. The bronchus should not be dissected clean of its peribronchial areolar tissue, nor should the mucosa be disturbed in any way. As a rule, the bronchial artery should be ligated at the cut end and should not be occluded in one

of the mattress sutures With a very thin cutting needle, mattress sutures of fine silk or cotton should be placed so that one leg of the suture passes around a cartilaginous ring (Fig 32) The space between the legs of the mattress sutures should not be too narrow for fear of producing a slough from stangulation of tissue between them The legs of the mattress may be

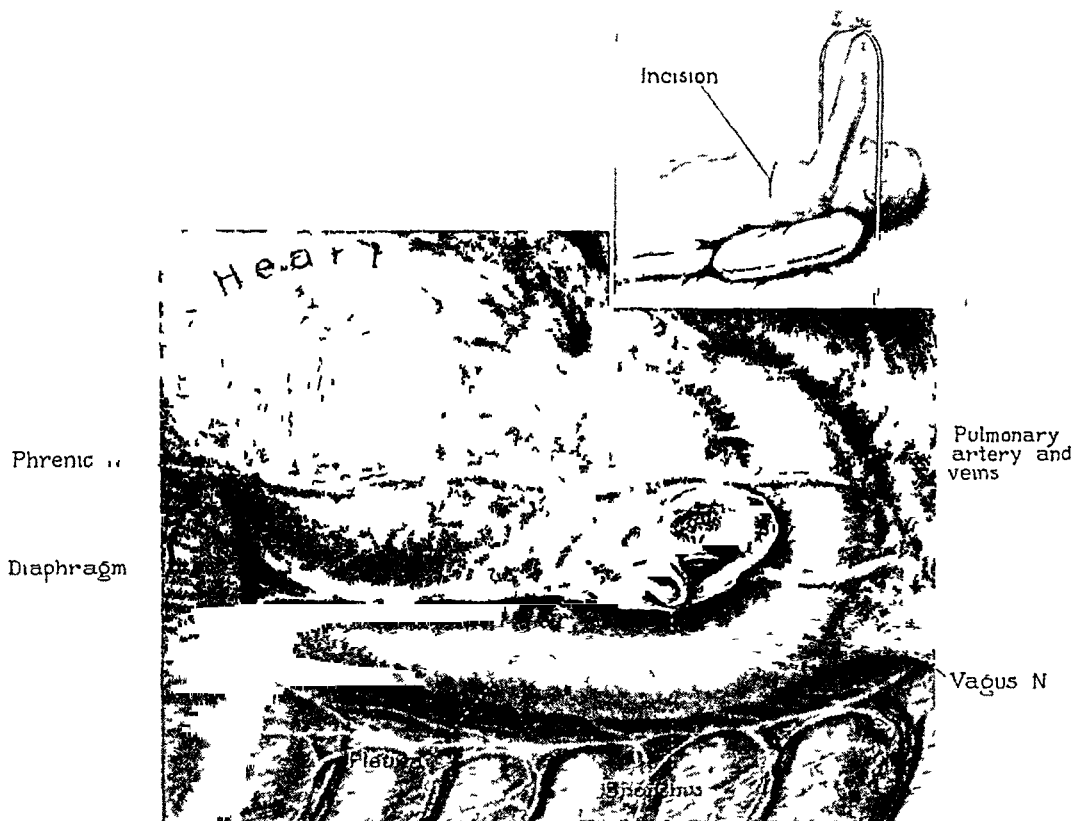


FIG 33—Shows relation of amputated stump which has been closed by mattress sutures high up near the bifurcation of trachea, open cuff of bronchus distal to suture line lying well within mediastinum

roughly 4 or 5 Mm apart, particularly in the posterior membranous portion They are placed postero-anteriorly and then back again anteroposteriorly (Fig 33) As a rule, six mattress sutures will suffice to close the bronchus completely This closure should always be checked by filling the thoracic cavity with warm salt solution above the level of the closed bronchial stump and then increasing the intratracheal pressure If the closure is not air-tight, bubbles will immediately appear

As few sutures as possible should be used in order to preserve the circulation and thus the viability of the cut end This cut end, not the area where the suture line is inserted, is the site of healing, and, therefore, constitutes the keystone to the arch of bronchial suture The sutures are only used as a stop-gap to prevent air from blowing to-and-fro during respiration while

CLOSURE OF BRONCHUS

the all-important cut end is healing. The suture line in the bronchus should be placed as high up on the stump as possible, that is, near the bifurcation of the trachea. The reason for this is two-fold, if the sutures cut through or if they form localized areas of infection, these areas will be as far removed from the healing end of the stump as possible, and, secondly, when the

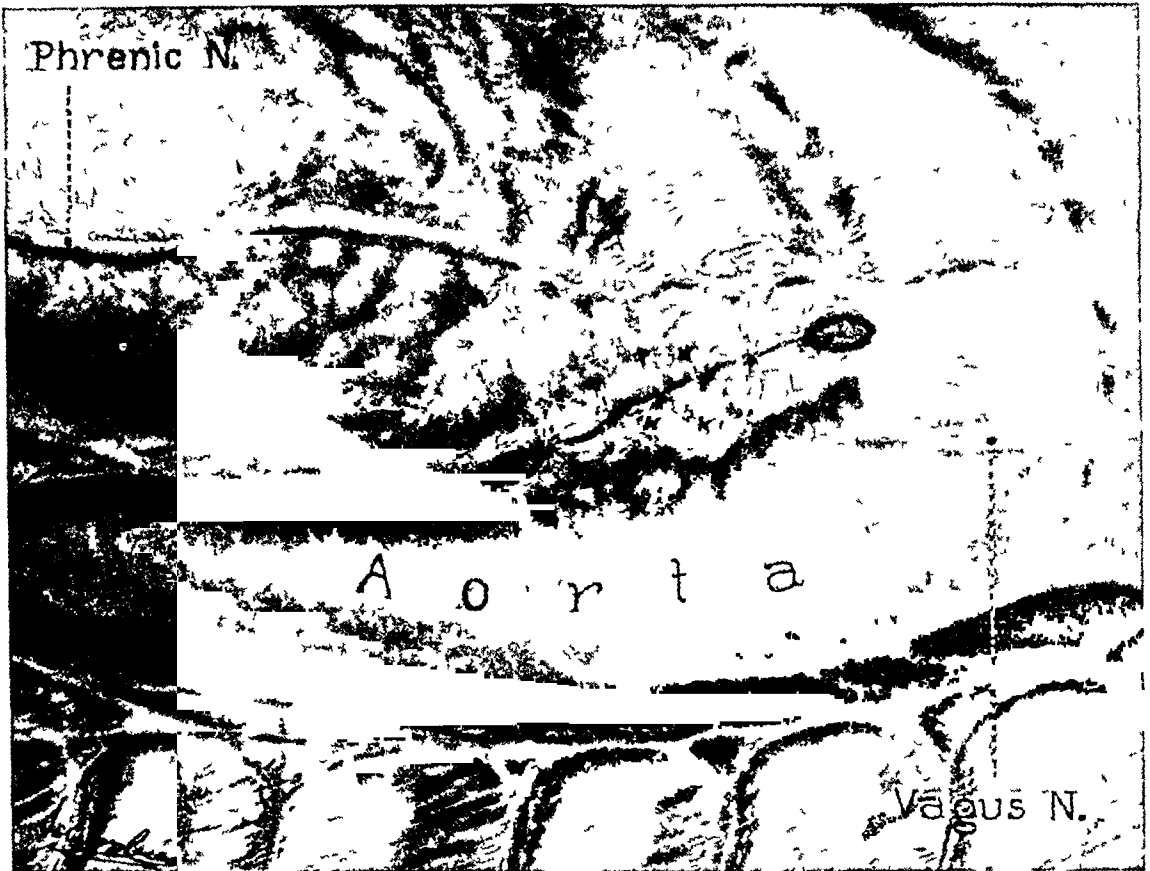


FIG 34—Denuded area containing hilar structures covered over by mediastinal pleura. Interrupted silk sutures closing lips of pleura except at either end. Four sutures, apart from those closing incision in the mediastinal pleura, hold nonserous surface of mediastinal pleura in apposition to cut end of bronchus.

sutures are placed near the trachea there is less likelihood of interfering with the bronchial artery. It is hazardous to place any form of suture in the cut end of the bronchus because no matter what the suture material, it constitutes an infected foreign body which will prevent primary agglutination and healing of the cut end. It has been shown experimentally and corroborated by human postoperative autopsy specimens, that the bronchus heals in the human being as it does in the dog, therefore, sutures, regardless of the method of insertion or type of material, will become infected and will cut. In the vast majority of instances the bronchus will not heal as it was sewed at operation, but will open up to a greater or less extent and heal by second intention. The bronchial stump, therefore, should be covered over with mediastinal pleura, as well as neighboring areolar tissue. At first, great difficulty was experienced in obtaining enough mediastinal pleura, particularly on the left side, to cover the stump. With patience, the pleura covering the aortic arch and the first portion of the descending thoracic aorta can be

dissected off and sutured over the stump. As there is apt to be a space remaining between the end of the bronchial stump and the sutured mediastinal pleura because of the bulging of the aorta into the thoracic cavity, it would seem advisable to approximate the pleura carefully to the cut end by placing two sutures, anteriorly and posteriorly, superficially in the peribronchial

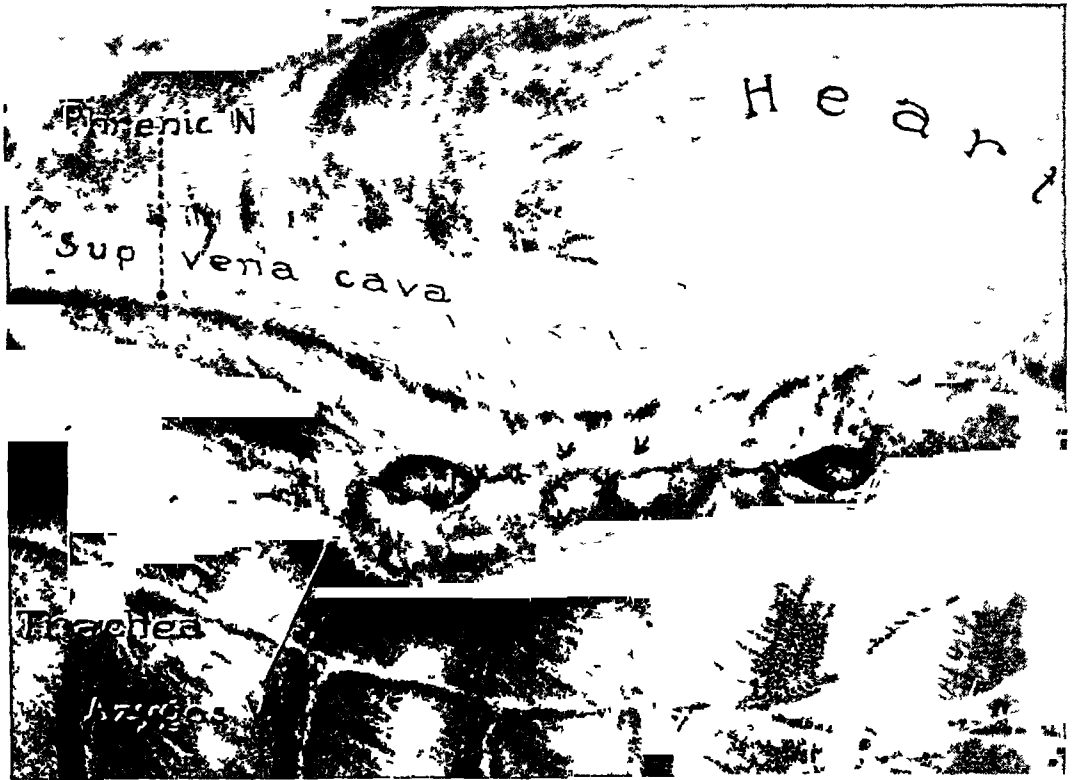


FIG 35—Shows same type of closure on right side as Figure 34, on left side

fibrous tissues, proximal to the cut end. This ensures prompt apposition of the cut end of the stump to the overlying mediastinal pleura, or areolar tissue. In the human being the mediastinal shift is not so immediate or so extensive as in the dog so that other means to accomplish this end, such as sutures, must be resorted to (Figs 34 and 35). If only an upper or lower leaf of mediastinal pleura is available it should be used. The stump may be sutured down to the tissue immediately anterior to the vertebral column or the wall of the esophagus may be employed on the left side as well as the outer covering of the pericardial sac. On the right side the mediastinal pleural membrane is usually more abundant, but in two cases in which a considerable amount had to be sacrificed in the removal of the tumor, the azygos vein was ligated, divided, and sutured over the bronchial stump. Likewise, in one case a sufficient length of the pulmonary artery distal to its ligated portion was available for covering the stump of the bronchus on the left side. Mediastinal pleura is to be preferred, but when unprocurable other tissues may be substituted. The apposition of the mediastinal pleura over the cut end of the bronchial stump should be as



FIG 36—Method of pulling mediastinal pleura over open cuff of bronchus peripheral to the suture line when there is scarcity of mediastinal pleura

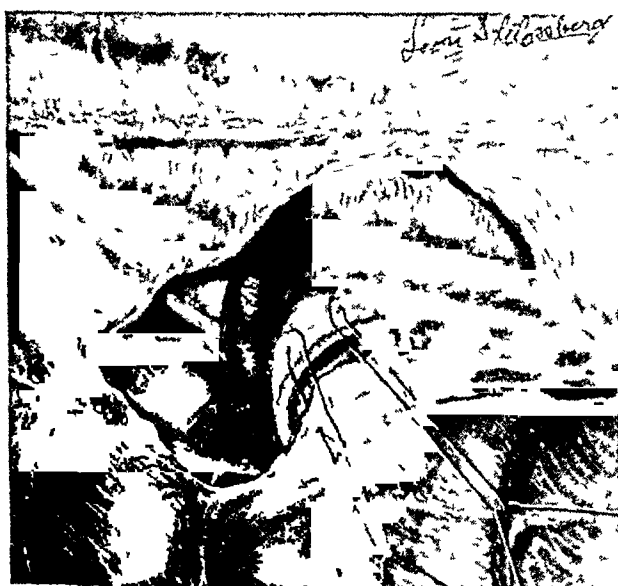


FIG 37—Another method of elevating a flap of mediastinal pleura to cover over bronchial stump

snug as possible, but openings ought to be left at either end of the suture line so that if air should leak from the bronchus an avenue of escape will have been provided (Figs 35 and 36) In a few recent cases sulfanilamide has been dusted in the area about the bronchial stump before closure of the chest (Fig 37)

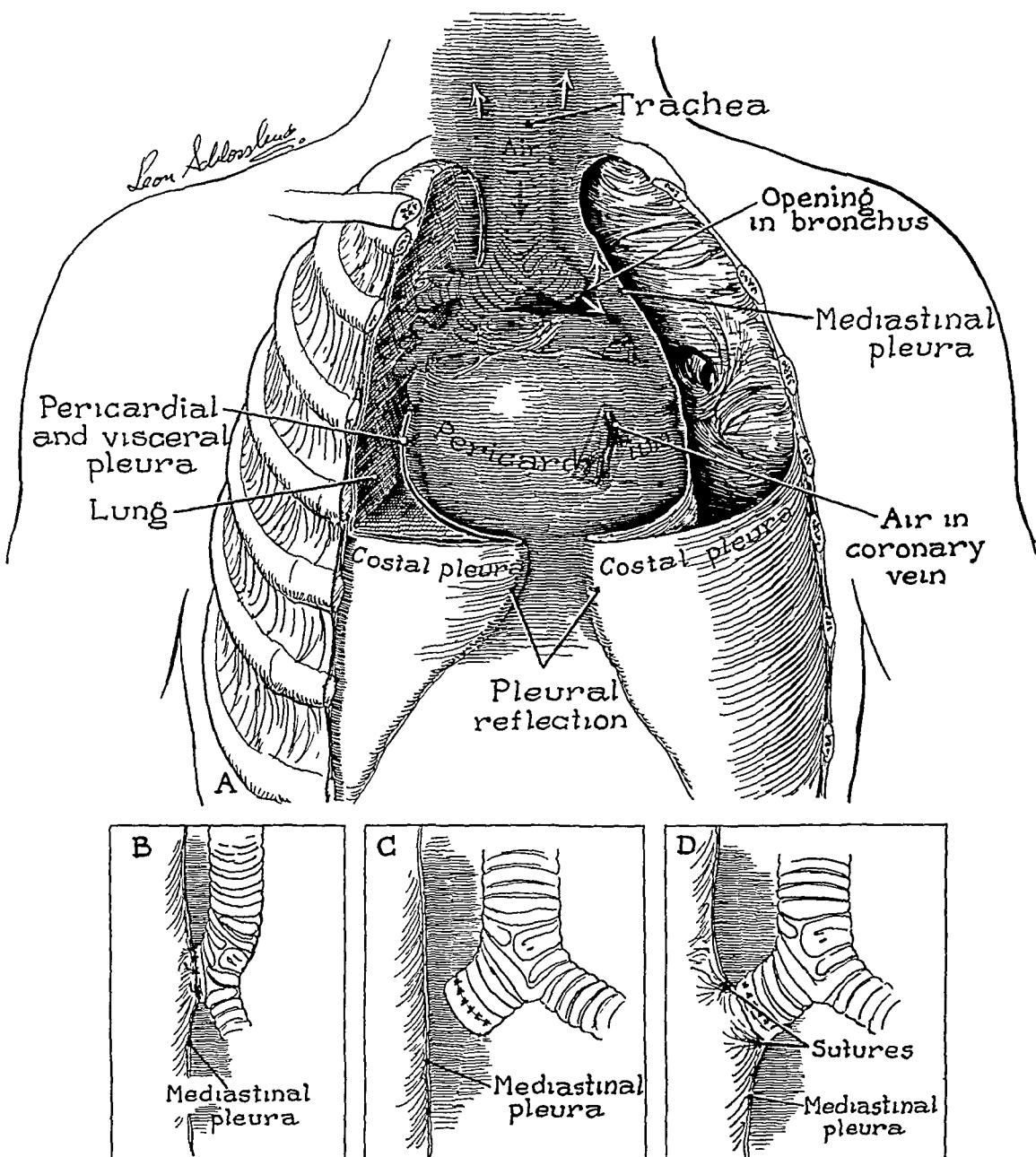


FIG 38—A Shows point at which air emboli were found in coronary veins, mediastinal emphysema the result of air leaking into mediastinum unable to escape except along tissue planes marked by white arrows Sterile fibrous thorax already formed on operated side B Closure of mediastinal pleura over right bronchial stump in dog Note close apposition of stump to mediastinal pleura, due to sutures and flexibility of mediastinum in dog C Space left, in patient above described, between mediastinal pleura and stump of bronchus D Proper apposition of bronchial stump in human, accomplished by superficial sutures in peribronchial fibrous tissue

Two of the three deaths that have occurred in the last 27 cases of total pneumonectomy were due to leakage from the bronchus after closure by the method above described. In each, however, a technical error was made that would seem to explain the death. In one, the bronchus was clamped across before amputation with a curved Kelly clamp in order to use this as a handle to pull on the hilus. After the bronchus was cut across the clamp slipped off, and it is believed that the occluding sutures were unintentionally placed through this devitalized area. The end of the bronchus sloughed, and the patient died of a massive empyema. Since that time no clamps of any type have been used. If feasible, bronchial occlusion sutures may be placed before amputation of the lung. In the second case the mediastinal pleura was sutured tightly and completely across the hilar defect on the left side, but was not properly brought into apposition with the bronchial stump. Thus, a space was left in the mediastinum with no avenue of escape for air if the bronchus should leak. Leakage occurred on the eighth day after a previously uneventful afebrile convalescence. Mediastinal emphysema, followed by extensive subcutaneous emphysema, developed. After three days, or on the eleventh postoperative day, when the patient seemed to be improving, he suddenly died. At autopsy an embolus was observed in the anterior coronary veins (Fig. 38). The bronchus had opened, but the air could not escape. There was an enormous mediastinal emphysema. The bronchus had been closed with silk sutures as usual, and it is believed that if the mediastinal pleura had been brought into apposition with the cut end of the stump the bronchus would not have leaked. Furthermore, an opening at each end of the sutured mediastinal pleura should have been left for the escape of air. It is well to note here that mediastinal or subcutaneous emphysema or both may give rise to air emboli.

CONCLUSIONS

From this study it seems likely that the main point of healing of the bronchus is at the cut end. Every effort must be made to preserve the viability of this portion, not only by gentle handling, which avoids any form of trauma, such as crushing, cauterization, or suturing, but also by preserving the circulation in the bronchial artery. The greatest attention should be given to the placing of the occlusion sutures, particularly the number, so that interference with the circulation of the stump will be as little as possible. If the circulation is cut off, the entire end of the cuff distal to the suture line, or at least part of it may slough. Primary agglutination of this open end is thus prevented, so that when any of the occluding sutures give way a bronchial fistula develops at once. After amputation, and following the placing of the mattress sutures, it is well to allow the bronchial artery to bleed while the sutures are being tied in order to avoid occluding this vessel in one of the stitches. The bronchial stump should be brought into apposition with nearby or contiguous viable tissue, preferably mediastinal pleura. The mediastinum should not be closed tightly about the stump, but an

avenue provided for the escape of air in the event that the bronchus opens. The use of occluding nonabsorbable sutures is advocated as a means of closing the bronchial tube for a sufficient length of time to permit healing of the cut ends.

The suture line should be placed as far proximal to the cut end of the stump as possible and the minimal number of sutures employed to effect an air-tight closure. There apparently is no method or type of suture that can be relied upon of itself to secure permanent occlusion and healing of the bronchus as it had been sewed at operation. There is no autopsy evidence of this in the human being, and healing at the suture line occurred in only 18 per cent of the experimental animals, a percentage so low that the possibility of such type of healing cannot be regarded as likely in the great majority of instances. The granulation and later fibrous tissue which brings about closure of the cuff-like open end of the bronchial stump is derived mainly from the bronchial walls. In some individual instances, in both the human being and the experimental animal, the entire bronchial wall would be drawn toward the center of the lumen and sometimes actually inverted into the bronchial stump by the contracting granulation tissue, but in the majority of cases the cylindrical open end of the bronchus was filled with a mass or plug of granulation tissue that successfully occluded the stump. The bronchial epithelium grew across the closed end as a modified or somewhat flattened cell-type.

Finally, it would appear that the most important steps in the procedure to effect solid healing of the bronchus are, first, to occlude the amputated stump with as few sutures as will prevent the passage of air long enough to permit sufficient healing of the cuff of bronchus distal to the suture line, second, to avoid in every way devitalization of the terminal end of the amputated stump, and third, to effect an intimate apposition between the cut end and the surrounding areolar tissue, preferably mediastinal pleura.

REFERENCES

- ¹ Gluck, F. Experimentelles Beitrag zur Frage der Lungenextirpation. Berl Klin Wchnschr, 18, 645, 1881.
- ² Block. Experimentelles zur Lungenresection. Deutsche med Wchnschr, 7, 634, 1881.
- ³ Biondi. Lungenextirpation bei experimenteller lokalisirter tuberculose. Wien med Jahrb, 1, 207, 1884.
- ⁴ Willard, D. F. Experiments in Pneumonectomy and Pneumotomy. Tr. Coll Physicians, 13, 133, 1891.
- ⁵ Murphy, J. B. Surgery of the Lung. J A M A, 31, 151, 1898.
- ⁶ Tiefel, M., and Mitt, A. D. Experimentelle studien uber Lungen and Pleura-Chirurgie. Grenzgeb d Med u Chir, Supplement 3, 789, 1907.
- ⁷ Frederick, P. L. Uber den Raumosgleich in der Brusthohle nach einseitiger Lungenamputation. Arch f klin Chir Bull, 27, 647, 1908.
- ⁸ Danielson, W. Beitr zur Lungenchirurgie. Bronchotomie und Lungenresection. Beitr f klin Chir, Tubing, 60, 94, 1908.
- ⁹ Robinson, S. ANNALS OF SURGERY, 47, 184, 1908.
- ¹⁰ Halsted, W. S. Clinical and Experimental Contributions to Surgery of the Thorax. Tr Am Surg Assn, 27, 119, 1909.

- ¹¹ Meyer, W Pneumonectomy with Aid of Differential Air Pressure J A M A , 53, 119, 1909
- ¹² Robinson, S, and Sauerbruch, F Untersuchungen ueber die Lungenextirpation Deutsche Ztschr f Chir , 102, 542, 1909, Zentralbl f Chir , 37, 391, 1910
- ¹³ Quinby, W C, and Moise, G W Experimental Pneumonectomy and Application to Man Boston M & S J , 165, 121, 1911
- ¹⁴ Galle Lungenchirurgie Garre und Quincke, 1912
- ¹⁵ Henschen, K Experimente zue intrathorakalen Lungenchirurgie Beitz z klin Chir , 41, 1433, 1914
- ¹⁶ Gieitz, K H Über Extirpation von Lungen und Lungenlappen mit Versorgung des Bronchialstumpfes durch frei transplantierte Fascia Lata Zentralbl f Chir , 41, 1433, 1914
- ¹⁷ Kawamura, H Experimentelle studien ueber die Lungenextirpation Deutsche Ztschr f Chir , 131, 189, 1914
- ¹⁸ Heuer, G J, and Dunn, G R Experimental Pneumonectomy Bull Johns Hopkins Hosp , 31, 37, 1920
- ¹⁹ Bettman, R B Experimental Closure of Large Bronchi A Study of the Factors Concerned in Failure of the Bronchi to Heal Arch Surg , 8, 418, 1924
- ²⁰ Feiermann, J Zur Versorgung des Bronchialstumpfes nach Lungenamputation Arch f klin Chir , 137, 300, 1925
- ²¹ Bettman, R B, James, W A, Tannenbaum, K, and Slobe, E Closure of the Bronchi in Lobectomies Surg Gynec & Obst , 46, 602, 1928
- ²² Joannides, M Care of Stump in Pneumonectomy and Lobectomy Arch Surg , 17, 91, 1928
- ²³ Schleuter, S A, and Weidlein, I F Experimental Lobectomy and Pneumonectomy Arch Surg , 13, 459, 1926
- ²⁴ Nisson, R Simplification of Excision Deutsche Ztschr f Chir , 219, 389, 1929
- ²⁵ Adams, W E Subtotal Atelectasis and Pneumonectomy in Dogs Proc Soc Exper Biol & Med , 28, 957, 1931
- ²⁶ Blalock, A Studies on Bronchial Occlusion by the Method of Adams and Livingston Surg Gynec & Obst , 56, 779-781, 1933
- ²⁷ Longacre, J J Experimental Pneumonectomy Jour Thoracic Surg , 4, 587, 1934-35
- ²⁸ Thomas, L C, Behrend, A, and Mann, F C Experimental Pneumonectomy Jour Thoracic Surg , 6, 677, 1936-37
- ²⁹ Taffel, M Repair of Tracheal and Bronchial Defects with Free Fascia Grafts Surgery , 8, 56, 1940
- ³⁰ Rienhoff, W F Graded Pneumonectomy in the Treatment of Tumors of the Lung Bull Johns Hopkins Hosp , 64, 167-194, 1939
- ³¹ Stafford, E S Experimental Pneumonectomy with Obliteration of the Bronchial Stump Jour Thoracic Surg , 10, 480, 1941

DISCUSSION—DR EVARTS A GRAHAM (St Louis, Mo) I agree fully with Dr Rienhoff that the question of securing permanent closure of the bronchus is one of the major problems confronting us with the technical features of the operation of total pneumonectomy I agree also fully with him that the operation of total pneumonectomy is probably going to be done more and more The chief indication for it will be bronchogenic carcinoma which as you all know is a very common disease It is not a very unusual condition, but it is at least of the same order of frequency as cancer of the colon, including the rectum, and probably is even of a greater order of frequency

The difficulties that confront one in the closure of the bronchus as he has said, are chiefly again in my experience, on the right side There is not nearly so much difficulty on the left side

These experiments which have been shown have been most illuminating to me I had not realized that in the closure of the bronchus, that apparently stayed closed when closed by mattress silk sutures, a method which I have used in recent years, these silk sutures did

cut through so frequently, as he has indicated. My difficulty in using mediastinal pleura, as he has represented so beautifully on these drawings, has been of several sorts. In the first place it is not easy by any means to find mediastinal pleura that can be drawn over. The pleura is, of course, exceedingly thin. It is so thin that it is transparent. One cannot put any tension on it whatever without tearing it. I have succeeded several times in getting what I thought was an effective closure of the bronchus with mediastinal pleura, with a method somewhat similar to what he has described, and have seen the pleural flap tear out when the patient had a violent cough or an unusually violent inspiratory act.

Dr Churchill some time ago asked me why I did not use free pleural transplants as he had used them with considerable success. I confess I had not tried it until he suggested it to me because I did not think it would work, but since his suggestion to me I have tried it on a number of cases and I have found that I have had a fair degree of satisfaction with it.

I have also tried pedicle-flaps from the pleura of the chest wall with the idea that they would preserve the circulation longer. I have had a fair degree of success with those but still the problem remains.

Now I think that one of the fundamental difficulties about the healing of the bronchus is not only the anatomic features and the question of having it covered with pleura, but the question of infection. If all of the bronchi in the human being which we had to close were as sterile as those of the dog there would be less difficulty with the permanent closure but in most cases in which a pneumonectomy is indicated there is infection present and infection of a highly virulent type. With anaerobic putrefactive organisms the sulfonamide drugs at least in my experience are ineffective, and I know of no application of any antiseptic substance of any sort which is effective in a practical manner that is to say, in any manner in which it can be applied to the prevention of infection in these cases.

Consequently, I fear that unless one can devise some more certain method than I know anything about at the present time, we are still going to have to face this very difficult problem of subsequently breaking open the bronchial stump with infection of the pleural cavity.

That brings me to one thing more, which concerns the remarks that I made when I was discussing the previous papers. One way to prevent a serious infection from an open bronchial stump is to do a thoracoplasty at the time of the total pneumonectomy, which will eliminate any pleural cavity to be infected.

The dangers of the simultaneous thoracoplasty coincident with the total pneumonectomy I have already alluded to, but from the ideal standpoint if we could do safely a thoracoplasty at the same time as a total pneumonectomy I do not think the question of closure of the bronchial stump would continue to be anything of major importance.

Now, just a word or two more. This perhaps is dragging things in a little bit by the "coat tail" but I hear among groups of people who are not familiar with what has been going on in chest surgery great pessimism expressed about the operation of total pneumonectomy, particularly with reference to carcinoma of the bronchus. Consequently, I always like to seize upon an opportunity to do a little propaganda. There is a feeling. What difference does it make whether you do a pneumonectomy or not on a patient with bronchogenic carcinoma? You are not going to get anywhere anyway. He is going to die pretty soon of cancer. What is the use of operating upon him and subjecting him to all this trouble?

I would like to say that in my own experience now I have one patient perfectly well and living nine years afterward, another patient six years and five months afterward, another patient five years, five patients, three years, and a very considerable number less than that who are living and apparently free from any evidence of recurrence of carcinoma. It seems to me that these figures are sufficiently good evidence of the fact that the operation is worth while and that it is essential, therefore, that we go on and develop to as good a point as possible technical perfection, so that the mortality will be less.

Dr Blades and I have had 76 total pneumonectomies. Of these, 59 were for bronchogenic carcinoma, and 17 for other conditions. Although the operation must still be regarded as a very serious one we are pleased that our operative mortality is steadily declining. During the period beginning with January 1, 1939, we have had 48 cases of total pneumonectomy for bronchogenic carcinoma with 18 hospital deaths (a mortality of 37 per cent). When the operation is carried out for conditions other than carcinoma the mortality is considerably less. In 17 noncancer cases there were four hospital deaths (a mortality of 23 per cent).

CLOSURE OF BRONCHUS

DR NORMAN S SHENSTONE (Toronto, Canada) A year ago in Toronto, at the meeting of the American Association for Thoracic Surgery, I described a simple method of closing the bronchus after pneumonectomy. I should like to show the illustrating slide to this association, and also to report the results we have obtained.

(Slide) In the technic that we follow the dissection of all the other structures of the hilus is carried out before dealing with the bronchus. We believe that by this sequence the operation is made easier and the danger of infection reduced to a minimum. The bronchus is divided about one-eighth of an inch distal to a pair of light Kocher-style of forceps applied as close as possible to the trachea and the cut margins are approximated anteroposteriorly by three interrupted sutures of fine silk supplemented by a running suture of catgut. Following this procedure the stump is powdered with sulphathiazole, displaced into the mediastinum, and finally covered by pleura.

We have operated upon 23 consecutive cases by this method, seven for carcinoma, five for adenoma and seven for various forms of tuberculosis, mostly bronchial stenosis. In only one of these has an open fistula developed and that in a case of very active unilateral tuberculosis, in which the bronchus opened two weeks after the primary operation. I do not believe that the method of closure can be blamed in this particular case, because it was a very doubtful case for surgery.

DR ALTON OCHSNER (New Orleans, La.) I would like to emphasize one point and that is one which has not been mentioned yet, namely, a cause of failure of closure of the bronchus which we have encountered. Out of the series of 32 total pneumonectomies for pneumoplastic disease we have had three cases in which there has been a failure of closure. Two of these have been in patients who have had extensive preoperative irradiation. We feel at the present time that this is a definite contraindication to surgery.

The only other patient in whom we have had difficulty, as far as closure is concerned, was a patient in whom we could not satisfactorily pleuralize the mediastinum. The simplicity with which this can be accomplished is exemplified by some experiments that Dr. De Bakey, in our clinic, has done. He has shown in animals that the simple closure of the bronchus by means of a silver clip, similar to the clip the neurosurgeons use, will satisfactorily close the bronchus and satisfactory healing will occur. We have never had quite enough nerve to try this in humans, but I am sure it would be true.

The technic that we have used has been very much the same as Dr. Shenstone's. We have used a crushing clamp, and applied mattress cotton sutures, sutures proximal to the crushing clamp. After removing the clamp and tying these sutures, we put in through-and-through sutures over the end. But we have been extremely careful, and have been influenced by Dr. Rienhoff's earlier papers in regard to this, to pleuralize the wound. If we could not accomplish it with a flap, we did it with a free graft, and have had no occasion to fear this method of closure, except in those cases in which there has been extensive irradiation.

DR ALFRED BLALOCK (Baltimore, Md.) I think that Dr. Rienhoff, because of lack of time, did not state the number of experiments which he performed in which no sutures whatever were placed in the bronchus. I have been fortunate in seeing some of these experiments, and I must say I should not have thought previously that one would be able to produce an air-tight closure of the bronchus simply by approximating with several sutures the thin pleura which lies near the end of the divided bronchus. It is obvious that in the case of patients Dr. Rienhoff does not recommend an omission of sutures in the bronchus. Even though the sutures in the bronchus may not hold permanently, in most instances they allow time for the pleura to heal over the end of the bronchus.

The importance of this paper to me is that it is a fundamental study in wound healing in which the particular tissue happens to be the bronchus.

DR FRANK H. LAHEY (Boston, Mass.) I particularly wanted to wait until the thoracic surgeons had completed their remarks before I arose, solely in the interests of war surgery, with the idea that the small note regarding cardiac arrest for 20 minutes with complete recovery without cerebral damage, which was recently published in the Journal of the American Medical Association, might not have been observed by some of the members of this Association. I am very sure that if this war goes on we may all possibly have to do war surgery, involved in which will be some thoracic surgery. The event which occurred in our clinic undoubtedly has previously occurred and will occur again and again.

that is, complete cardiac arrest during lobectomy I am not aware, however, that its successful management has ever been accomplished and reported before

I believe it is valuable for everyone to have in mind how feasible it is by cooperation between the anesthetist and the surgeon, with the patient's chest open, to maintain circulation so that at least as occurred in this single case no cerebral damage will result with an arrest of the heart for a period of 20 minutes This is not a case in which there was any doubt Anesthesia records accurately kept and observations by competent men with the patient's chest open substantiate the certainty of these facts

Here is a case in which perhaps as a result of the vagovagal reflex all cardiac action ceased for 20 minutes but with the anesthetist Dr Hand producing artificial breathing with the anesthesia bag one could demonstrate, with the chest open that the expansion of the lung filled the heart and substituted for the diastole and with Dr Herbert Adams the surgeon contracting the heart manually produced the systole With these manipulations circulation was maintained cardiac action was completely restored at the end of 20 minutes and the patient recovered with complete mental clearness A negative electro-encephalogram was obtained and now the patient is entirely well over a period of months

I again wish to state that this accident will happen in thoracic surgery that it will happen in war surgery and it is extremely important for us all to remember that it is possible by cooperation between an anesthetist and a surgeon either with the patient's chest open or through the diaphragm to manually maintain circulation while efforts are being made to restore cardiac action

DR WILLIAM F RIENHOFF JR (closing) I would like to thank Dr Blalock for his discussion, and I will first answer his question, because in my haste as he suggested, I neglected to mention the data which he has called attention to The second series consisted of 48 dogs and as in the first series there were no operative deaths or instances of leakage of the bronchus notwithstanding the fact that no sutures were used to occlude the blind end of the bronchus There were in this series two deaths from distemper In the dog there is always an abundance of mediastinal pleura which is ready at hand and not the slightest difficulty was ever experienced in obtaining a sufficient amount to cover the end of the bronchus As Dr Blalock suggested we do not advocate using only the mediastinal pleura in human beings, but wish to emphasize that this is a very important step in the closure of the bronchus following total pneumonectomy in the human being and it should be pointed out that it is our opinion that interrupted mattress sutures of nonabsorbable material preferably of silk or cotton, should be used to occlude the airway or primary bronchus in the human and considered only a temporary measure until the vital end of the blind end of the stump has had sufficient time to become occluded by the healing of its own and contiguous tissue in the mediastinum One should abstain from all forms of trauma such as cauterization, any type of crushing or even the placing of sutures in the end of the cuff

In answer to Dr Graham it is of course possible that in some cases particularly on the left side adequate mediastinal pleura may not be available for satisfactory covering of the bronchial stump In our recent cases the last 30 to be exact, of total pneumonectomy in the human due to a more deliberate and painstaking mobilization of the pleura we have not experienced any difficulty in being able to close over the raw area of the hilus of the lung with this membrane Particularly is this true if the hilar structures are uninvaded If the structures are invaded it is very questionable whether one should attempt to do a total pneumonectomy It is possible to dissect the mediastinal pleura on the left side off the anterior surface of the aorta mobilize it from the anterior surface of the aorta as well and obtain enough to subtent this space inside the curvature of the aorta, thus bringing this posterior leaf of mediastinal pleura sufficiently forward to suture it to the anterior leaf It is necessary also in this event to suture the pleura to the peribronchial fibrous tissue so that the end of the cuff and nonserous surface of the pleura are brought into intimate contact In regard to Dr Graham's suggestion about thoracoplasties we have not found it necessary to perform thoracoplasties at the same time or previous to the total pneumonectomy However in three cases when postoperative bronchial fistulae developed resulting in a rather large infected dead space occupying part of the former pleural cavity it was necessary to perform a posterior thoracoplasty in three stages This procedure was completely successful in obliterating the dead space and bringing about closure of the bronchus undoubtedly because of the approximation of the lateral chest wall to the mediastinal surface Unquestionably in Dr Graham's experience thoracoplasties have relieved some

respiratory difficulties in patients which he has discussed in the past, and I am certain that his experience in this respect is far greater than mine. Undoubtedly this procedure is a most valuable one as an adjunct in certain cases of total pneumonectomy.

Ultimately the conclusion will probably be that the majority of human beings who have a total pneumonectomy will not need a thoracoplasty, but there are unquestionably quite a number that either because of respiratory difficulties, postoperative discomfort or postoperative infection will be benefited by such a procedure.

It is very interesting that Dr. Shenstone's experience with closure of the bronchus has been quite successful, indeed, although the technic that he has employed has varied considerably from the one that we have discussed. I cannot help reiterating that I think the main point of healing of the bronchus after amputation regardless of the type of sutures used is in, and at the cut end, certainly in the great majority of instances. Dr. Shenstone's results, although his series of cases is very small, would suggest that as in many other surgical procedures dealing with other organs in the body that there are several ways of accomplishing a thing successfully.

THE EFFECT OF PNEUMONECTOMY UPON CARDIOPULMONARY FUNCTION IN ADULT PATIENTS* †

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IN RECENT YEARS pneumonectomy has become an accepted method of treatment of malignant and benign tumors of the bronchus, and of various types of chronic pulmonary suppuration. Clinical experience has repeatedly demonstrated that the surgical ablation of one of a pair of as vitally important organs as the lungs is compatible with survival and maintenance of a fairly high degree of physical activity. Studies on the physiologic effect of pneumonectomy, until recently,^{1, 2} have been almost exclusively experimental. The observations of Biemer³ on cats, and of Longacre, Carter, *et al*,^{4, 5} on dogs are best known. It was shown by Longacre, Carter, *et al*, in a series of experiments covering several years, that age at the time of the lung resection influences (1) the subsequent behavior of the dogs under conditions of physical stress, and (2) the later development of hyperplasia and/or emphysema in the remaining lung. However important these experiments may be, to extend their conclusions to human subjects would fail to recognize fundamental differences encountered in experimental and clinical conditions. For example, the highly mobile mediastinum of the dog has not its counterpart in man, and, in the latter, the remaining lung is quite frequently already the site of pathologic changes. Aside from information of theoretic interest regarding the immediate and remote effects of pneumonectomy upon pulmonary function, physiologic studies in man may be of practical value in individual cases, chiefly in helping to decide which are the most favorable conditions for the maintenance of a high degree of functional efficiency in the remaining lung. They may be especially contributory to the problems of optimum position of the mediastinum and of supplemental thoracoplasty. During the past several years, on the Tuberculosis Service at Bellevue Hospital, under a grant of the Commonwealth Fund, a method for the study of pulmonary function and of cardiocirculatory function, insofar as it is related to the former, has been developed,⁶ and the tests devised were used in various chronic pulmonary diseases and in surgical chest conditions^{7, 8}. Already, reports have been made upon the late effect of pneumonectomy in children,¹ and the immediate postoperative influence of pneumonectomy upon the state of respiratory gases in the arterial blood of adult subjects.² The present report, based upon a

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study of 12 subjects, is concerned with various physiologic problems arising as a result of pneumonectomy performed in adults

Material for Study—Physical characteristics and clinical data concerning the 12 subjects studied have been tabulated in Table I. There were one

TABLE I
PHYSICAL CHARACTERISTICS AND CLINICAL DATA ON THE 12 PATIENTS STUDIED

Pt	Sex	Age Yrs	Ht Cm	Wt * Kg	Body Surface* Sq M	Diagnosis	Time of Study†			Media- stinal Mobility‡	Follow-Up after Pneumonectomy
							\bar{a} pn	\bar{p} pn	\bar{p} Suppl Thoraco		
W J	M	53	160	54	1.48	Ca rt M L bronchus	+	+	+	+	Survival 2 years active
W W	M	64	175	64	1.78	Ca lt U L bronchus	+	+	0	0	Survival 18 mos, active
D M	M	62	178	57	1.72	Ca lt U L bronchus	+	+	0	++	Survival 15 mos active
T G	M	43	169	62	1.71	Ca rt main bronchus	+	+	0		Death—metastasis, 7 mos
E B	M	31	190	98	2.18	Ca lt main bronchus	+	+	0	+	Death—metastasis 20 mos
R B	M	60	175	55	1.65	Ca lt L L bronchus	+	+	0	0	Survival 1 year Metastasis chest wall
W H	M	47	168	72.5	1.82	Ca lt main bronchus	0	+	0	0	Death—metastasis 21 months
E R	M	32	174	54.5 53	1.66 1.64	Bronchiectasis left upper and lower lobe	+	+	+	0	Survival 9 mos Recent thoraco- plasty
A M	F	23	148	44.5 37.5	1.35 1.25	Bronchiectasis	+	0	+	0	Survival 12 mos, active
F I	M	46	178.5	70 65	1.88 1.82	Endobronchial lbc Obstruction rt main bronchus	+	0	+	0	Survival 9 mos, active
M K	M	37	169	66	1.76	Chronic lung abscess, rt	0	+	0	0	Survival 31 mos, active
K G	M	33	175	83	1.99	Traumatic frac- ture rt main bronchus with complete ob- struction	0	+	0	0	Survival 2 yrs active

*The two figures correspond to pre- and postoperative weight and body surface area

†Time of study— \bar{a} pn = before pneumonectomy

\bar{p} pn = after pneumonectomy

\bar{p} Suppl Thoraco = after supplemental thoracoplasty

‡Mediastinal mobility after pneumonectomy

female and 11 males, with ages from 23 to 64 years. Pneumonectomy was undertaken in seven instances after a diagnosis of carcinoma of the bronchus had been established, in three, for chronic suppuration of the lung, in one, after traumatic fracture of a main bronchus and resulting stenosis, and in one case, for almost complete obstruction of a main bronchus secondary to an endobronchial tuberculosis.

In six subjects the studies were carried out before pneumonectomy and at various intervals afterwards, when the patients had resumed normal activity, in two of these, studies were again repeated after a supplemental thoracoplasty had been completed. In two patients, studies were made before ablation of the lung and again after the pneumonectomy had been supplemented by a thoracoplasty, without measurements in the interval. In the four remaining cases measurements were made singly or repeatedly after pneumonectomy.

Method of Study—In Table II, information concerning the functions studied, and the measurements made, along with references regarding technics, normal control values, etc., have been summarized

Briefly stated, the measurements were as follows (A) Lung volumes and subdivisions, (B) maximum breathing capacity, (C) ventilation, breathing reserve, and respiratory gas exchange under basal conditions, during moderate exercise, and during a five-minute period of recovery following exercise,

TABLE II
SUMMARY OF MEASUREMENTS OF CARDIOPULMONARY FUNCTION

A VENTILATORY FUNCTION			
Measurement	Definition	Significance	References
<i>Lung Volume</i> in liters		Description of available air space for ventilation	Technics—formula for prediction of normal values according to body size age sex ^{9 10 11}
Vital Capacity (V C)	Volume of maximally deep breath		
Residual Air (R A)	Volume in lung after extreme expiration		
Total Capacity (T C) (T C = V C + R A)	Total volume in deepest inspiration		
R A	Residual air expressed as per cent of total capacity	Expression of degree of pulmonary distention physiologic or pathologic (emphysema)	
Ratio $\frac{\text{R A}}{\text{T C}} \times 100$			
<i>Maximum Breathing Capacity</i> —lit/min (M B C)	Maximum volume of air that can be displaced per minute	Estimation of the efficiency of the chest bellows in displacing air per unit of time	Technics ^{6 12} —formula for prediction M B C lit/min = $80.9 \times \text{B S in sq m} = 29.3$ Technic ⁶ Normal control values—according to age sex (unpublished data)
<i>Ventilation</i> in liters per min per sq m body surface (V)	Actual volume of air per minute displaced in a given physical state		
(1) Basal			
(2) Moderate exercise			
(3) During 5 minutes of recovery from moderate exercise			
<i>Breathing Reserve</i> (B R = M B C - V)	Excess breathing capacity beyond actual ventilation in a given state		
B R	Breathing reserve expressed as per cent of maximum breathing capacity	Provides a numerical estimation of dyspnea in pulmonary insufficiency	Relation with dyspnea ⁶ Normal control values according to age sex (unpublished data)
Ratio $\frac{\text{B R}}{\text{M B C}} \times 100$			
B ALVEOLORESPIRATORY FUNCTION			
Measurement	Definition	Significance	References
<i>Pulmonary Emptying Rate</i>	Nitrogen concentration of alveolar air after 7 minutes pure oxygen breathing	A numerical estimate of adequacy of inspired air distribution in alveoli	Technic and range of variation ¹¹
<i>Respiratory Gas Exchange</i>	Carbon dioxide output and oxygen intake in a given physical state expressed		Technic ⁶ Normal range according to age and sex (unpublished data)
(1) Basal	(a) in cc/sq m/min	(a) Measures amount of gas exchange used in a given physical state	
(2) Moderate exercise	(b) in cc/liter vent	(b) Gives efficiency of ventilation in providing O ₂ absorption (utilization)	
(3) During 5 minutes of recovery			
<i>State of Respiratory Gases in Arterial Blood</i>	(a) O ₂ hemoglobin saturation—%	Measures effectiveness of lungs in aerating blood and state of respiratory gases reaching tissues	Technic—Normal range ⁶
(1) Basal	(b) Carbon dioxide pressure—mm Hg		
(2) During early recovery from moderate exercise			

Measurement	C CARDIOPULMONARY FUNCTION		References
	Definition	Significance	
Includes			
(a) <i>Routine</i>			
Arterial blood pressure			
Electrocardiogram			
Ballistocardiogram			
(b) <i>Cardiovascular response to rapid intravenous saline infusion</i>	(a) Variation of venous pressure (b) Circulation time (c) Vital capacity following infusion of 1500 cc isotonic solution in 30 min	Brings out latent congestive state due to back pressure from failure of left heart of pulmonary vascular bed or of right heart	Technic ^{6 13 14}

(D) state of respiratory gases in the arterial blood at rest and immediately after completion of the moderate exercise, and (E) variations in venous pressure, circulation time, and vital capacity following an increase in blood volume produced by a rapid intravenous infusion of 1500 cc of a saline solution. Data available from the literature⁹ and a separate study of 60 normal subjects, age 20 to 69, supplied the desired control values.

Results—Four separate headings may better describe the data obtained in this study:

(1) State of pulmonary and cardiocirculatory function after pneumonectomy in comparison with normal subjects

(2) State of ventilatory function before and after pneumonectomy in same subjects

(3) Influence of thoracoplasty supplementing a pneumonectomy upon the state of ventilatory function

(4) Influence of mediastinal adjustment and preexisting pulmonary emphysema upon pulmonary function

(1) State of Pulmonary and Cardiocirculatory Function after Pneumonectomy. Comparison with Normal Subjects—Data on ten patients are available, two subjects studied only after supplemental thoracoplasty was completed have been excluded. The ten patients have been separated into two groups according to age. Group I consists of six patients, ages ranging from 32 to 47. Group II consists of four patients, ages ranging from 53 to 66.

The predicted normal figures and the control normal figures were calculated according to data available in subjects in the same age-groups. Mean values, observed, predicted, or calculated for controls, are tabulated in Tables III to IX.

A—VENTILATORY FUNCTION

1 Lung volumes and subdivisions (Table III, Chart 1)

In both groups I and II, the mean size of the remaining lung in deepest inspiration is somewhat larger than the predicted size of one of a pair of normal lungs. This increase is due to the persistence of a large residual air volume, the remaining lung after pneumonectomy is slightly smaller at the end of a complete expiration than two normal lungs in Group I, and as large as two normal lungs in Group II. There is then evidence of lung distention after

pneumonectomy, especially in the older age-group, although the mean residual air of 37 per cent of the total capacity does indicate that if pulmonary emphysema is present, it is of mild degree, or present only in a small proportion of the group. Studies of individual data prove the latter to be the case.

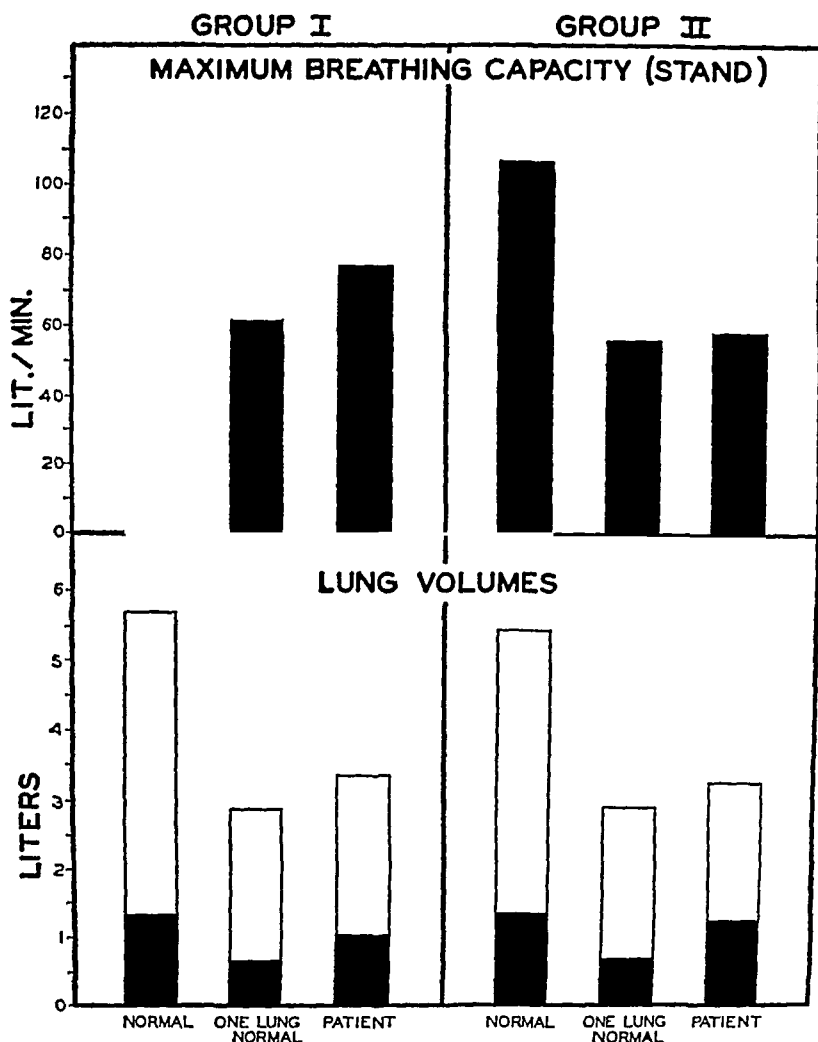


CHART 1—Lung volumes and subdivisions in liters, and maximum breathing capacity in liters per minute. In each of the two groups, the blocks to the left = average predicted values for normal subjects of same size, sex, and age distribution, the blocks in the center = the average assumed value for one lung of the normal subjects, the blocks to the right = average observed values in patients studied after pneumonectomy. Under lung volumes, solid blocks = residual air volume, white blocks = vital capacity (complemental air + reserve air).

2 Maximum breathing capacity in liters per minute (Table III, Chart 1)

The maximal efficiency of the chest bellows in displacing air after pneumonectomy is reduced in both groups. In Group I the maximum breathing capacity is 63 per cent of the predicted value for two normal lungs, and in Group II 50 per cent. In the younger age-group, coincident with less distention, the remaining lung is more effective in circulating air than the remaining lung in the older age-group, and in addition is more effective than one of a pair of normal lungs, (maximum breathing capacity 26 per cent greater than predicted value for one lung).

SEQUELAE OF PNEUMONECTOMY

TABLE III
LUNG VOLUMES* AND MAXIMUM BREATHING CAPACITY AFTER PNEUMONECTOMY

Group	Total Capacity (liters)	Vital Capacity (liters)	Residual Air (liters)	$\frac{R}{T+C} \times 100$	Maximum Breathing Capacity—Standing (liters/minute)
	Mean	Mean	Mean	Mean	Mean
Group I†					
Predicted					
Both lungs	5 68	4 44	1 28	22 5	121 4
One lung	2 84	2 22	0 64		60 8
Observed	3 35	2 32	1 03	30 8	76 6
Group II†					
Predicted					
Both lungs	5 45	4 12	1 33	24 4	106 0
One lung	2 86	2 16	0 70		55 8
Observed	3 25	2 03	1 33	37 5	57 8

*Saturated dry gas at 37° C and prevailing barometric pressure

†Group I consists of 6 patients, age 32 to 47 and Group II of 4 patients age 53 to 65

Average predicted and observed values in two groups of adults after pneumonectomy

3 Ventilation at rest, during moderate exercise, during each of five minutes of recovery (Table IV, Chart 2)

There are significant differences between the two groups. In the younger age-group the average figures of ventilation under varying states of activity are almost identical with the average control normal figures, in the older age-group, ventilation is somewhat larger than normal at rest, much more so during exercise and during recovery.

TABLE IV
VENTILATION AT REST*, DURING MODERATE EXERCISE AND DURING EACH OF FIVE MINUTES OF RECOVERY FROM MODERATE EXERCISE AFTER PNEUMONECTOMY

Group	Ventilation liters/min /sq m B S *						
	Basal Mean	Exercise Mean	Rec 1 Mean	Rec 2 Mean	Rec 3 Mean	Rec 4 Mean	Rec 5 Mean
Group I†							
Normal controls	3 42	9 72	12 80	8 30	7 50	6 13	5 40
Patients after pneumonectomy	3 28	9 88	12 84	8 32	7 52	5 60	5 26
Group II†							
Normal controls	3 92	11 13	14 83	10 83	8 37	7 08	6 20
Patients after pneumonectomy	4 17	15 11	15 35	13 02	10 25	8 65	7 62

*Saturated gas at 37° C and prevailing barometric pressure

†See Table III

Average observed values in two groups of adults after pneumonectomy, and average values in two corresponding groups of normal subjects

TABLE V
BREATHING RESERVE
RATIO $\frac{\text{BREATHING RESERVE}}{\text{MAXIMUM BREATHING CAPACITY}} \times 100$ AT REST DURING MODERATE EXERCISE,
AND DURING EACH OF FIVE MINUTES OF RECOVERY AFTER PNEUMONECTOMY

Group	Breathing Reserve						
	Ratio $\frac{\text{Breathing Reserve}}{\text{Maximum Breathing Capacity}} \times 100$						
	Basal Mean	Exercise Mean	Rec 1 Mean	Rec 2 Mean	Rec 3 Mean	Rec 4 Mean	Rec 5 Mean
Group I*							
Normal controls	94 0	83 7	76 0	83 4	86 9	88 9	90 2
Patients after pneumonectomy	89 3	76 0	59 4	75 4	80 2	83 5	84 1
Group II*							
Normal controls	91 2	79 6	67 4	76 4	81 4	84 4	86 2
Patients after pneumonectomy	86 5	51 7	49 3	57 4	66 8	71 2	74 9

*See Table III

Average observed values in two groups of adults after pneumonectomy and average values in two corresponding groups of normal subjects

4 Ratio $\frac{B \cdot R}{M \cdot B \cdot C} \times 100$, at rest, during exercise, during each of five minutes of recovery (Table V, Chart 2)

This ratio being dependent upon the values of maximum breathing capacity and of ventilation, it is not surprising to find it lower in the older age-group

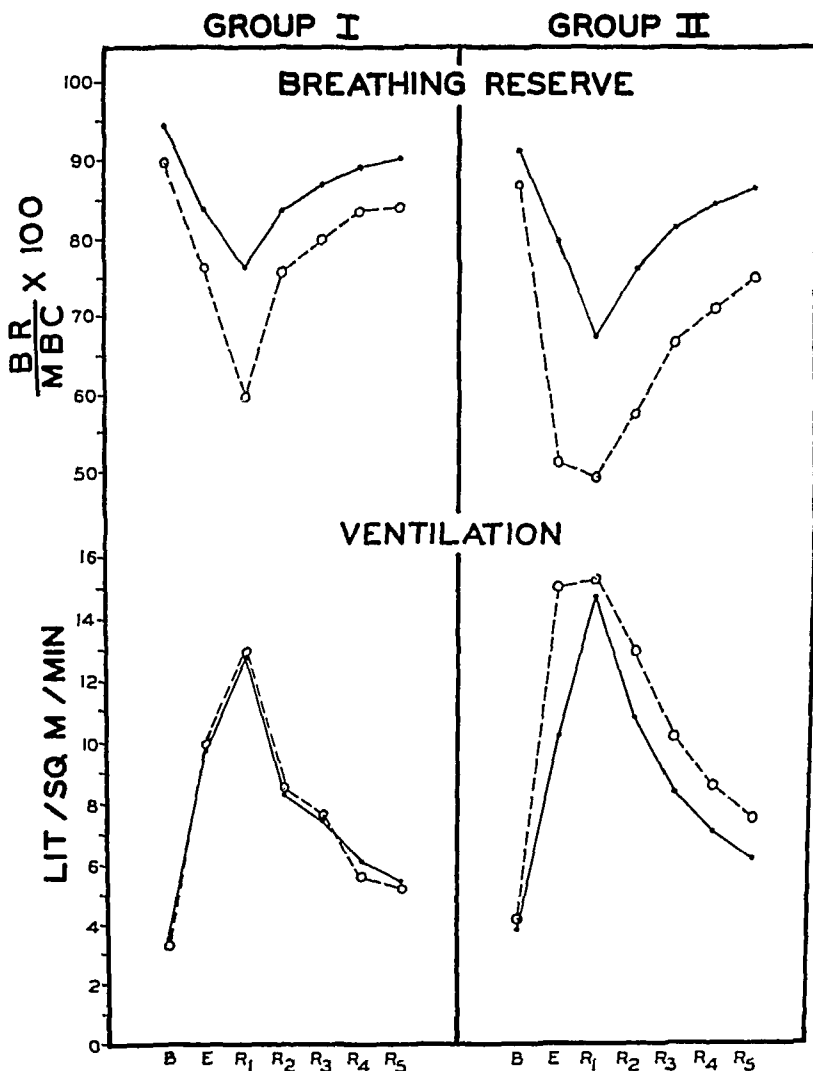


CHART 2—Ventilation and ratio $\frac{\text{breathing reserve}}{\text{maximum breathing capacity}} \times 100$

under standard basal conditions (B) during moderate exercise (E), and each of the five minutes of recovery following moderate exercise (R₁ = 1st minute of recovery, R₂ = second minute, etc.) Solid lines = average values for normal subjects, age 30 to 50 (Group I), and 51 to 69 (Group II). Broken lines = average values in 10 patients after pneumonectomy in same age groups

than in the younger, especially during exercise and during the recovery period from exercise. As dyspnea usually occurs when the value of this ratio is below 60 to 70 per cent, it should be more marked and more persistent for the same degree of activity in Group II than in Group I. This is supported by observations concerning dyspnea made in both groups during the recovery period—in Group I the average duration of dyspnea following completion of the standard exercise was 33 seconds, in Group II it was 142 seconds.

Summarizing the main findings concerning the anatomic status of the remaining lung, and its ventilatory function, in ten patients after pneumonectomy (a) The lung was somewhat distended, more so in the older group, (b) maximal efficiency of the chest bellows in displacing air with only one lung was better than predicted in the younger subjects, but just exactly as predicted in the older age-group, and (c) relative hyperventilation was present during exercise and persisted during the recovery period in the older subjects, and it further encroached upon the breathing reserve and resulted in a greater tendency to dyspnea

B—ALVEOLORESPIRATORY FUNCTION

1 Pulmonary emptying rate Following pneumonectomy, the average figures of nitrogen concentration in alveolar samples taken after seven minutes of pure oxygen breathing in Groups I and II, as well as individual figures, were well within normal range. Tidal air, in spite of a definite increase in residual air volume, was thus efficiently distributed during quiet breathing to the functioning alveoli of the remaining lung

2 Respiratory gas exchange—carbon dioxide output and oxygen intake (Table VI and VII)

TABLE VI

Group	RESPIRATORY GAS EXCHANGE AND DURING FIVE MINUTS OF RECOVERY FROM MODERATE EXERCISE			CARBON DIOXIDE OUTPUT AT REST* DURING MODERATE EXERCISE AFTER PNEUMONECTOMY		
	CO ₂ Output cc /min /sq m B S †			CO ₂ Output, cc /liter vent		
	Basal	Exercise	Recovery	Basal	Exercise	Recovery
Group I ‡						
Normal controls	104	329	1516	35.4	36.8	42.5
Patients after pneumonectomy	107	336	1449	36.7	37.6	40.4
Group II ‡						
Normal controls	104	329	1523	30.5	34.0	37.5
Patients after pneumonectomy	101	374	1601	27.9	28.5	33.2

*Under basal conditions

†Dry gas at 0° C and 760 mm Hg barometric pressure

‡See Table III

Average observed values in two groups of adults after pneumonectomy, and average values in two corresponding groups of normal subjects

TABLE VII

Group	RESPIRATORY GAS EXCHANGE DURING FIVE MINUTES OF RECOVERY FROM MODERATE EXERCISE			OXYGEN INTAKE AT REST* DURING MODERATE EXERCISE AFTER PNEUMONECTOMY		
	O ₂ Intake cc /min /sq m B S †			O ₂ Intake cc /liter vent		
	Basal Mean	Exercise Mean	Recovery Mean	Basal Mean	Exercise Mean	Recovery Mean
Group I ‡						
Normal controls	134	489	1523	45.8	57.3	43.4
Patients after pneumonectomy	143	520	1524	49.1	57.5	42.9
Group II ‡						
Normal controls	130	491	1509	38.1	52.5	36.9
Patients after pneumonectomy	126	475	1438	34.9	36.7	31.0

*Under basal conditions

†Dry gas at 0° C and 760 mm Hg barometric pressure

‡See Table III

Average observed values in two groups of adults after pneumonectomy and average values in two corresponding groups of normal subjects

There are significant differences between the two groups. The average figures in Group I are but little different from the normal control values—

the direction in changes being, if anything, toward greater rather than lesser efficiency during periods of physical activity. In Group II, however, the carbon dioxide output, per minute, was larger than in the control group during exercise and recovery, and the oxygen intake per minute less during corresponding periods, hence there is evidence that efficiency in gas exchange is impaired. Particularly significant are the low rate of oxygen removal per liter of ventilation at rest and during recovery from exercise, and its total lack of increase during exercise. Two causes may be invoked to explain these changes: (a) Inefficient alveolar ventilation due to hyperventilation, and (b) inadequate increase in circulation during exertion and the following recovery period.

3. State of respiratory gases in arterial blood (Table VIII). In both groups the proportion of hemoglobin in the oxyhemoglobin state, and the tension of carbon dioxide in the blood leaving the lung, were well within normal range both at rest and after moderate exercise. This indicates that during moderate exertion the correlation between alveolar ventilation and pulmonary circulation and/or the diffusion across alveolocapillary membranes remained normal.

TABLE VIII
ARTERIAL BLOOD STATE OF RESPIRATORY GASES AT REST AND DURING EARLY RECOVERY
FROM MODERATE EXERCISE AFTER PNEUMONECTOMY

Group	Oxyhemoglobin Saturation %				CO ₂ Tension in Mm. Hg			
	Rest		Recovery		Rest		Recovery	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Normal	96.2	±1.2	95.8	±1.3	43.7	±3.5	43.0	±2.4
Group I*								
Patients after pneumonectomy	95.5		94.8		39.8		37.4	
Group II*								
Patients after pneumonectomy	95.9		94.6		39.8		40.9	

*See Table III

Average oxyhemoglobin saturation % and CO₂ pressure in Mm. Hg in two groups of adults after pneumonectomy and normal range

Summarizing the data on gas exchange after pneumonectomy, the only abnormality noted among the ten patients after they had resumed some activity was, in the older patients, lowered efficiency in supplying oxygen to the tissues, especially during exertion and the early recovery period. The repayment of the oxygen debt, contracted during exercise, takes longer than in the younger patients in spite of the tendency to hyperventilation noted during the short period of observation. Whether this is due to poorer alveolar ventilation occurring under stress in a lung somewhat distended, or inadequate increase in cardiac output cannot be decided on the basis of data obtained, the aeration of the blood leaving the lung remained, however, well within normal range.

C—CARDIOCIRCULATORY FUNCTION

Routine measurements of cardiocirculatory function including arterial blood pressure, electrocardiogram, and ballistocardiogram, failed to reveal any abnormality that might be connected directly to the surgical removal of the lung. One of the older subjects with auricular fibrillation, present prior to the pneumonectomy, rallied remarkably after operation, and there was no

evidence that "minimal myocardial damage," as revealed by the electrocardiogram in a few patients, was increased to any significant degree. Insofar as the infusion test was concerned (Table IX), it failed to bring out any latent congestive state due to back pressure from failure of the left heart, pulmonary vascular bed or right heart. In addition, the initial venous pressure level and the circulation time were well within normal figures, the slightly lower figures for venous pressure in Group II are of no significance, being probably due to inaccurate prediction of the exact position of the right auricle in subjects with chest inflation greater than normal.

TABLE IX
STATE OF CIRCULATION, VENOUS PRESSURE, CIRCULATION TIME, AND VITAL CAPACITY BEFORE AND AT END OF INFUSION TEST (1500 cc SALINE IN 30 MINUTES) AFTER PNEUMONECTOMY

Group	Venous Pressure		Circulation Time		Vital Capacity
	Mm H ₂ O		sec		% Decrease
	Before Infusion Mean	At End of Infusion Mean	Before Infusion Mean	At End of Infusion Mean	At End of Infusion Mean
Normal range	Below 90	Increase less than 60 Mm H ₂ O or final level less than 125 Mm	Below 18 sec	Below 20 sec	Less than 8%
Group I					
Patients after pneumonectomy	64	78	15.7	17.1	5.0
Group II					
Patients after pneumonectomy	32	46	14.3	15.9	4.6
Average observed values in two groups of subjects after pneumonectomy and normal range					

In the results so far presented, the most significant findings in patients after pneumonectomy, besides an obvious decrease in size of the lungs, were (a) A greater tendency to dyspnea in a group of subjects age 53 to 65, due to a greater decrease in the chest bellows' capacity for circulating air and a greater demand upon ventilating requirements during and following moderate exercise, and (b) a lesser efficiency in the same group to supply oxygen to the tissues during and following exercise. There was some evidence that lung distention is more a liability than an asset, both from the point of view of mechanics of the chest bellows and of gas interchange between alveoli and circulating blood.

(2) State of Ventilatory Function Before and After Pneumonectomy in the Same Subjects—To decide whether some of the findings described in the previous section may be, to some degree, unrelated to the surgical ablation of the lung itself and the intrathoracic adjustments which followed, it is important to compare data obtained before and after pneumonectomy. Such observations were made in six patients, two of them with pathology throughout an entire lung before pneumonectomy (E. B. and E. R.), and the remaining four with pathology limited to one lobe or less (W. J., V. W., D. M., and T. G.). Changes in vital capacity and residual air in the first two patients were insignificant (within 180 cc). The maximum breathing capacity in E. B. increased by 14 liters per minute after pneumonectomy. For the other four subjects absolute decrease in vital capacity and in residual air volumes was large, as one expected, averaging 1.2 liters for vital capacity and 0.7 liters for the residual air. But, significantly enough, the percentage of the residual air in

the total capacity remained practically unchanged—38 per cent before and 40 per cent after. As three out of four of these patients belonged to Group II of the preceding section it seems, therefore, that the somewhat larger degree of lung distention noted in older subjects after pneumonectomy antedates the surgical procedure. Another interesting observation is that as the average vital capacity in these four patients decreased by 34 per cent after pneumonectomy, the average maximum breathing capacity decreased by only 21 per cent.

(3) Influence of Thoracoplasty Supplementing a Pneumonectomy upon the State of Ventilatory Function—In four patients pneumonectomy was supplemented by a thoracoplasty. In two (W J and E R), measurements were made before and after pneumonectomy and again after thoracoplasty, in the other two (F I and A M), the lung removed being functionless, measurements made before pneumonectomy were repeated only after thoracoplasty and resumption of activity.

Data summarizing many observations on W J (Tables X, XI and Plate I), cover prepneumonectomy, postpneumonectomy, and postthoracoplasty periods. Following pneumonectomy the maximum breathing capacity was reduced to about 50 per cent of the preoperative value, a rather considerable decrease, and, in addition, alveolar ventilation was apparently less efficient in

TABLE X
INFLUENCE OF THORACOPLASTY UPON LUNG VOLUMES AND MAXIMUM BREATHING CAPACITY
IN FOUR PATIENTS AFTER COMPLETION OF PNEUMONECTOMY

Patients		State	Total Capacity (liters)	Vital Capacity (liters)	Residual Air (liters)	R A ——— T C	× 100	Maximum Breathing Capacity— Standing (liters/minute)
W J	male	Before pneumonectomy	6 22	4 07	2 15	34 5		90 9
age 55		After pneumonectomy	3 63	2 14	1 49	41 1		45 8
		After thoracoplasty						
		1 month	2 86	1 92	0 94	33 0		65 6
		6 months	3 23	2 00	1 23	38 2		58 2
F I	male	Before pneumonectomy	4 13	2 98	1 15	27 9		59 8
age 46		After thoracoplasty	2 88	1 92	0 96	33 4		77 7
A M	female	Before pneumonectomy	2 59	1 74	0 85	32 8		34 8
age 23		After thoracoplasty	1 96	1 24	0 72	36 7		37 0
E R	male	Before pneumonectomy	3 51	2 66	0 85	24 2		72 9
age 32		After pneumonectomy	3 38	2 36	1 02	30 2		67 4
		After thoracoplasty	3 13	2 25	0 88	28 0		64 0

TABLE XI
INFLUENCE OF THORACOPLASTY UPON BREATHING RESERVE AND RATE OF O₂ INTAKE AT REST
DURING MODERATE EXERCISE AND DURING RECOVERY FROM MODERATE EXERCISE
IN ONE PATIENT AFTER PNEUMONECTOMY

Patient	State	Breathing Reserve							Rate of O ₂ Intake		
		Ratio $\frac{\text{Breathing Reserve}}{\text{Maximum Breathing Capacity}} \times 100$							cc /lit vent		
		Rest	Exercise	1 min	2 min	3 min	4 min	5 min	Rest	Exercise	Average of 5 min Recovery
W J	Before pneumonectomy	91 0	79 6	59 1	69 8	75 6	83 0	85 0	39 2	49 1	30 7
	After pneumonectomy	86 4	53 7	53 9	61 6	71 0	75 6	79 5	36 4	37 1	32 8
	After thoracoplasty										
	6 months	89 8	69 6	59 3	69 2	71 8	79 9	81 2	41 4	43 1	36 2

supplying oxygen for tissue needs. It was thought that a plausible explanation for the unfavorable functional result was moderate relative overdistention of the remaining lung as successive measurements had shown a steady increase of the percentage of residual air in the total capacity. To control this distention thoracoplasty was decided upon. One month after its completion the percentage of residual air in the total capacity had returned to the prepneumonectomy level and the maximum breathing capacity was nearly 20 liters larger than before thoracoplasty. In subsequent months some of these gains were partly reduced as scoliosis tended to develop, but as some beneficial effects still remained, dyspnea was less marked after exercise than it was during the prethoracoplasty studies and the efficiency in providing oxygen absorption was considerably improved.

In patients F. I. and A. M. the influence of thoracoplasty is more difficult to evaluate because no data are available of the state of the pulmonary function after pneumonectomy. It is, however, suggestive that thoracoplasty little impaired the ventilating function as in both cases, especially F. I., the maximum breathing capacity after thoracoplasty was larger than before pneumonectomy.

In patient E. R., lung volume measurements and maximum breathing capacity were practically unchanged after pneumonectomy and after thoracoplasty.

It appears, therefore, that thoracoplasty after pneumonectomy does not impair further the mechanics of the chest bellows, and if scoliosis is successfully controlled, it may well improve pulmonary function by preventing lung overdistention.

(4) Influence upon Pulmonary Function of Mediastinal Adjustments and Preexisting Pulmonary Emphysema—Among the 12 patients studied there was only one who exhibited any significant clinical evidence of pulmonary emphysema before pneumonectomy. This man also presented a very difficult problem of mediastinal adjustment, and management of the remaining lung. D. M., age 62, was first studied, November 16, 1940 (Plate II, No. 1), after a carcinoma of the left upper lobe bronchus had been diagnosed and verified by biopsy. Lung volume measurements confirmed the clinical impression of pulmonary emphysema and the high ratio of residual air ($\frac{RA}{TC} \times 100$) indicated a marked degree of emphysema. Other measurements revealed that there was a considerable limitation in maximum breathing capacity, that oxygen absorption was not efficiently managed at rest or during increased physical activity, and that the arterial oxyhemoglobin saturation was somewhat below normal.

After pneumonectomy was performed the patient had to be kept in an oxygen tent for a period of three weeks, and suffered from obvious symptoms of anoxia as soon as he breathed atmospheric air. On December 14, 1940, (Plate II, No. 2) the residual air of the remaining right lung was almost exactly equal to that of both lungs prior to pneumonectomy. It constituted 71 per cent of the total capacity, indicating an extreme degree of emphysema.

Patient W J

I
4/25/40

II
11/4/40

III
6/17/41

IV
12/15/41



6 22	3 63	2 86	3 23
4 07	2 14	1 92	2 00
2 15	1 49	0 94	1 23
34 5	41 1	$\frac{R}{T} \times 100$	38 2
90 9	45 8	Maximum Breathing Capacity (lit/min)	58 2

Influence of thoracoplasty performed after pneumonectomy upon lung volumes and maximum breathing capacity
I Before pneumonectomy II After pneumonectomy III One month after thoracoplasty IV Six months after thoracoplasty

SEQUELAE OF PNEUMONECTOMY

Patient D VI

I

11/16/40



501
236
265

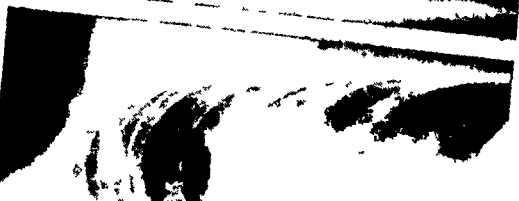
530

378

907

II

12/14/40



359

104

255

710

841

PLATE II

III

12/28/40



6994



68847

IV

11/13/41



Total Capacity/(liters)
Vital Capacity/(liters)
Residual Air/(liters)

283

133

150

R A

T C

X 100

528

Maximum Breathing
Capacity (lit/min)

4-6

Arterial Oxyhemoglobin
Saturation at Rest (%)

914

347
199
148

Influence of the state of lung distention upon various measurements of pulmonary function
I Before pneumonectomy, II After pneumonectomy, III Few days later,
after air replacement in left chest IV One year later, after oleothorax

displacement of trachea into left chest

Defective alveolar ventilation at that time resulted in low oxygen saturation in the arterial blood. Obviously the distention of the remaining emphysematous lung, clinically characterized by a deviation of the trachea to the left and a very low right diaphragm, was not of a compensatory nature. Physiologically, it was undesirable, and, anatomically, it was probably related to low total pressure of gases in solution in the fluid filling the deserted left hemithorax and subsequent distention of the contralateral lung.

With the mediastinum back in midline following air replacement (Plate II, No. 3) the residual air decreased to 52.8 per cent, and the arterial oxyhemoglobin saturation returned to preoperative value.

In order to maintain the mediastinum in the midline, oil was introduced and substituted for air and fluid. Frequent check-ups have prevented recurring overdistention of the right lung. One year later (Plate II, No. 4) with slight evidence of shift of the mediastinum *towards the right side*, and probably because of better muscular tone the maximum breathing capacity with one lung was almost identical to values obtained with two lungs, the percentage of residual air was lower than before pneumonectomy, and the arterial oxyhemoglobin saturation was normal. Concomitantly, the performance of the moderate exercise did not cause any more dyspnea than when the patient had two lungs.

The findings in this case suggest that the presence of emphysema is not an obstacle to satisfactory functional results if proper care is taken after pneumonectomy to avoid distention of the remaining lung.

DISCUSSION—In discussing the effect of pneumonectomy upon pulmonary and cardiocirculatory function in animals, and in man, early and late physiologic adjustments should be considered separately.

There is little data concerning the hemodynamic adjustments associated with the rapid rerouting of the entire stroke-volume of the right heart through the vascular bed of a single lung, in particular, no information regarding blood pressure changes in the lesser circulation, velocity of blood flow in the pulmonary circuit, *etc.* Yet the failure of proper adjustment in man is probably the most important cause of early postoperative death. It is announced by a syndrome resembling acute pulmonary edema oftentimes described as "drowned lung." The exact mechanism of this syndrome is unknown, its true nature even doubtful, some ascribing it to acute cardiac failure, others to acute pulmonary failure. The tests of cardiocirculatory function, described in this report, are of no avail in predicting, before operation, the chances that such a complication may develop. In one patient who died from "drowned lung," within 24 hours after pneumonectomy, the response to the infusion test performed prior to pneumonectomy had been absolutely normal.

In very rare instances a classical picture of cardiac failure developed after pneumonectomy in individuals entirely free of myocardial damage, arteriosclerotic heart disease, valvular disease, or without clinical manifestations of acute anoxia. The precipitating causes are altogether obscure and the development of cardiac failure is unpredictable.

The return of hemorespiratory gas exchange to a normal state following pneumonectomy was studied experimentally by Heuer and Andrus¹⁵. On the basis of technics available at the time their studies were made, these authors concluded that proper adjustments in respiratory gas exchange, under resting conditions, in dogs may be delayed one month or more. In man, a study of the carbon dioxide content and the oxyhemoglobin saturation made in our clinic² revealed that in the absence of complications the state of respiratory gases in the arterial blood was normal within a few days after pneumonectomy. In addition, this study showed that following lobectomy some degree of anoxia persisted for longer periods of time, possibly as a result of inadequate correlation between alveolar ventilation and pulmonary circulation in the remaining lobe on the operated side, as it reexpanded slowly. A persistent arterial oxyhemoglobin unsaturation after pneumonectomy may be due to three causes: (1) The presence of a large bronchopleural fistula, (2) a state of distention or compression of the remaining lung brought about by mediastinal shift, and (3) development of pneumonia in the remaining lung. The additional risk of anoxia during a period, so fraught with other hazards, requires that the variation of oxyhemoglobin saturation in the arterial blood should be carefully followed.

The late effects of pneumonectomy upon pulmonary and cardiocirculatory functions have been studied in great detail in dogs, operated upon as puppies or adult animals^{4, 5}. Recently these studies have to some extent been duplicated in children¹, and extended to adult man in the present report. In puppies and young children the surprising finding was that the capacity to perform exhausting exercise after pneumonectomy was comparable to that of the normal controls. In puppies, after pneumonectomy, there was enlargement of the remaining lung and histologic evidence of pulmonary hyperplasia. In young children hyperplasia was not demonstrated and the best performances were observed in those cases where the size of the remaining lung in forced expiration was not larger than predicted for one of a pair of normal lungs. The physiologic paradox of as good a performance with one lung as with two, under conditions of extreme physical demands, may be explained partly by the following considerations:

(1) Theoretically, it may be shown that the higher the ratio of tidal air to functional residual air, the more efficient is the mixing of gases in the alveoli. Such a situation arises after pneumonectomy—the dead space in the bronchial tree is reduced—the tidal air in one lung is larger, both combining to increase the efficient tidal air, and finally the functional residual air is smaller providing the remaining lung is not distended. (2) The tidal air is probably better distributed to ordinarily poorly ventilated lung areas, particularly around the hilum and at the apex, as the lung expands toward the opposite hemithorax in inspiration. (3) More blood circulates through the remaining lung as the functional diffusing surface for respiratory gas exchange is either increased in area by increase in the number of functioning capillaries or increased in efficiency by passage of more blood per unit of ventilated

alveoli. These considerations applying also to adults may well explain why respiratory gas exchange under conditions of moderate strain was efficiently managed in the younger group reported in the present paper.

In contrast to respiratory gas exchange ventilatory function is impaired in children and in adults after pneumonectomy. The breathing reserve under varying conditions of activity is lower than in normal subjects, and the tendency to dyspnea is greater. The reduction of ventilatory efficiency, however, is not proportional to the loss in lung volumes and to a considerable extent depends upon the degree of pulmonary distention.

The question of late development of pulmonary emphysema following pneumonectomy, performed during adult life, has not yet been settled because of lack of long follow-up. So far, our experience has been that when the mediastinum was maintained in its normal position, lung volume measurements failed to reveal evidence of developing emphysema. This situation, in humans, is entirely different from that encountered in dogs, where the distention of the remaining lung cannot be prevented. The shift of the mediastinum after pneumonectomy may be controlled by organization of the fluid in the empty hemithorax, by oleothorax, or by thoracoplasty. Our data tend to show that thoracoplasty does not reduce further the ventilatory function if measures are taken to keep the spine straight, and thus preserve the maximum expansion of the chest-bellows on the unoperated side. Postthoracoplasty scoliosis is highly detrimental to the efficiency of the chest-bellows mechanics, as has been demonstrated by previous work in tuberculous patients.⁷

No mention has been made, so far, in this report of bronchspirometry, which permits separate estimation of ventilation and gas exchange in each lung. In two cases with suppurative disease of the lung, this method was found to be of practical value in helping decide between limited and extensive lung resection.

SUMMARY

- 1 The effect of pneumonectomy upon pulmonary and cardiocirculatory function has been studied in 12 adult patients.
- 2 The following measurements have been made:
 - (a) Lung volumes and subdivisions
 - (b) Maximum breathing capacity
 - (c) Ventilation, breathing reserve, respiratory gas exchange, and state of the respiratory gases in the arterial blood, under basal conditions, during moderate exercise, and during the recovery period from moderate exercise
 - (d) Venous pressure, circulation time, and vital capacity before, during, and following an infusion of 1500 cc of a saline solution in 30 minutes
- 3 Ten patients, studied after pneumonectomy, were divided into two groups according to age, and compared to normal controls. Two of these ten patients were again studied after a thoracoplasty had been completed, and

two additional patients, not studied after pneumonectomy were studied only after thoracoplasty. Six of the ten patients, studied after pneumonectomy had already been studied before operation.

4 The chief difference between patients after pneumonectomy and normal subjects was the reduction in their breathing reserve in various states of activity. This reduction caused by a decrease in maximum breathing capacity was greater in the older patients because of the cumulative effect of abnormal hypoventilation.

5 The decrease in maximum breathing capacity was not proportional to the loss of lung volume, and was greatly influenced by the state of distention of the remaining lung.

6 The late effects of pneumonectomy upon gas exchange in the lungs, the state of respiratory gases in the arterial blood, and the cardiocirculatory function were insignificant.

7 In two patients, age 53 and 63, respectively, distention of the remaining lung due to mediastinal shift was detrimental to hemorespiratory gas exchange, especially in the older patient who had pulmonary emphysema.

8 A supplemental thoracoplasty in four patients did not impair, further, the ventilatory function, and in some patients was of distinct benefit.

9 Overdistention of the remaining lung following pneumonectomy, insofar as it impairs the mechanics of the chest bellows, and reduces the efficiency of gas exchange, is physiologically undesirable.

We wish to thank, particularly, Drs. Herbert C. Maier and Richard L. Riley for their assistance and many helpful suggestions.

REFERENCES

- ¹ Mestel, C. W., Cournand, A., and Riley, L. D. Pulmonary Function after Pneumonectomy in Children. *Jour Thor Surg* (In Press).
- ² Maier, H. C., Cournand, A. Studies of the Arterial Oxygen Saturation in the Post-operative Period after Pulmonary Resection. *Surgery* (In Press).
- ³ Bremer, J. L. The Fate of the Remaining Lung Tissue after Lobectomy or Pneumonectomy. *Jour Thor Surg*, 6, 336, 1937.
- ⁴ (a) Longacre, J. J., Carter, B. N., and Quill, L. McG. An Experimental Study of some of the Physiological Changes following Total Pneumonectomy. *Jour Thor Surg*, 6, 237, 1937.
(b) Carter, B. N., Longacre, J. J., and Quill, L. McG. A Study of the Changes in Cardiorespiratory Physiology following Total Pneumonectomy in Young Developing Animals. *Jour Thor Surg*, 7, 326, 1938.
- ⁵ Longacre, J. J., and Johansmann, R. An Experimental Study of the Fate of the Remaining Lung following Total Pneumonectomy. *Jour Thor Surg*, 10, 131, 1940.
- ⁶ Cournand, A., and Richards, D. W., Jr. Pulmonary Insufficiency. I. Discussion of a Physiological Classification and Presentation of Clinical Tests. *Amer Rev Tuberculosis*, 44, 26, 1941.
- ⁷ Cournand, A., and Richards, D. W., Jr. Pulmonary Insufficiency. II. The Effects of Various Types of Collapse Therapy upon Cardiopulmonary Function. *Amer Rev Tuberculosis*, 44, 123, 1941.
- ⁸ Cournand, A., Richards, D. W., Jr., and Maier, H. C. Pulmonary Insufficiency. III. Cases Demonstrating Advanced Cardiopulmonary Insufficiency following Artificial Pneumothorax and Thoracoplasty. *Amer Rev Tuberculosis*, 44, 272, 1941.

- ⁹ Kaltreider, N L, Fray, W W, and Hyde, H W Effect of Age on Pulmonary Capacity and its Subdivisions *Amer Rev Tuberculosis*, 37, 662, 1938
- ¹⁰ Darling, R C, Cournand, A, and Richards, D W, Jr Studies on the Intrapulmonary Mixture of Gases III An Open Circuit Method for Measuring Residual Capacity and its Subdivisions *Jour Clin Invest*, 19, 609, 1940
- ¹¹ Cournand, A Baldwin, E deF, Darling, R C, and Richards, D W, Jr, Studies on Intrapulmonary Mixture of Gases IV The Significance of the Pulmonary Emptying Rate, and a Simplified Open Circuit Measurement of Residual Air *Jour Clin Invest*, 20, 681, 1941
- ¹² Cournand, A, Richards, D W, Jr, and Darling, R C Graphic Tracings of Respiration in Study of Pulmonary Disease *Amer Rev Tuberculosis*, 40, 487, 1939
- ¹³ Caughey, J L Effect of Rapid Infusion on Venous Pressure A Test of Cardiac Reserve *Proc Soc Exper Biol & Med*, 32, 973, 1935
- ¹⁴ Richards, D W, Jr, Caughey, J L, Cournand, A, and Chamberlain, F L Intra venous Saline Infusion as a Clinical Test for Right-heart and Left-heart Failure *Trans Assn Amer Phys*, 52, 250, 1937
- ¹⁵ Heuer, G J, and Andrus, W deW The Alveolar and Blood Gas Changes following Pneumonectomy *Bull Johns Hopkins Hosp*, 33, 130, 1922

DISCUSSION —DR ANDRÉ COURNAND (New York) Physiologic studies after pneumonectomy in children show remarkable resemblance to the findings just reported by Dr Berry in adults I have studied, so far with Drs Charles W Lester and R L Riley the cases of five children after successful completion of pneumonectomy and return to normal life Two of the five children had a marked displacement of the mediastinum toward the operated side persisting after complete expiration Lung volume measurements show that the residual air volume of the single remaining lung of those two children was about the same as the residual air volume of two lungs of normal control This was in contrast to the other three children with mediastinum maintained in normal position where the residual air volume was about half that of the normal control Permanent overdistention of the remaining lung in the former group was associated with a much greater decrease in efficiency of the chest bellows for air displacement as in the latter This was conclusively shown by measurements of maximum breathing capacity As we have previously shown this measurement is the best means of estimating the breathing reserve which in turn, is closely related to intensity and development of dyspnea It was thus not surprising to find that the intensity and duration of dyspnea for varying degree of exertion were greater in the two children with permanent overdistention than in the three others These five children, during the performance of an exhausting type of exercise, showed remarkable efficiency in supplying oxygen to the tissues and displacing carbon dioxide from the circulating blood As a matter of fact with one lung these children were able to perform as much exercise as normal controls of same size and age their breathing reserve was still large enough to afford the required ventilation although at the expense of comfort as shown by greater degree of dyspnea and finally, their oxygen intake and carbon dioxide output were as large These observations confirmed the following concepts 1 That the breathing reserve in normal is well over and above any physiologic demand 2 That the limit to exhausting exercise is not ventilation but circulation

With Dr H C Maier we have studied the state of respiratory gas in the arterial blood during the immediate postoperative period following pneumonectomy This study revealed that the carbon dioxide content and the oxygen saturation in the arterial blood in the absence of complication, returns to normal within a few days after pneumonectomy This is in contrast with what is observed after lobectomy where some degree of anoxia persists for a longer period of time supposedly as a result of inadequate correlation between the ventilation and pulmonary circulation in the remaining lobe or lobes on the operative side

Persistent arterial oxygen unsaturation after pneumonectomy recognizes three possible causes First the presence of a large bronchopleural fistula second a state of distention or compression of the remaining lung brought about by mediastinal shift and third the development of pneumonia in the remaining lung The additional risk of anoxia during a period so fraught with other hazards requires that the variation of oxygen

saturation in the arterial blood should be carefully followed

As to the late development of pulmonary emphysema after pneumonectomy in children or adults, we have not yet settled the question, because of lack of long-following, but, so far, our experience has been that when the mediastinum is maintained in its normal position we failed to see any evidence of developing emphysema

In summary, we might state that overdistention of the remaining lung after pneumonectomy is not physiologically desirable, either in children, in adults, or in the older age-group. The teleologic concept, that the increase in size of the remaining lung to make up for the loss of the other lung, will bring about functional compensation, is not borne out by physiologic studies

DR EVARTS A GRAHAM (St Louis, Mo) Those who have not been primarily interested in chest surgery perhaps do not realize that there has been a very great deal of discussion and uncertainty in the minds of those of us who have been confronted by these problems, as to whether or not measures should be taken permanently to obliterate the empty space which is left after the removal of a lung

In my first case, which is just past the ninth anniversary—I know because my patient always calls me up on the fifth of April, and he called me up again this year to remind me—when I completed the operation I was alarmed at the huge empty space which remained, and I thought that the only thing to do was a thoracoplasty to obliterate it. Consequently, I at the same time removed seven ribs. The patient made an uneventful recovery, although I removed the remaining three ribs at a subsequent date about three weeks after the operation. I was greatly impressed with the ease of the convalescence of the patient. In fact, I demonstrated him at a meeting of the Clinical Surgical Society, which met at St Louis only about two weeks after his operation. He apparently had no dyspnea, and everything was going along very well.

Of course, this is a very radical procedure to add to the operation of pneumonectomy, and when Dr Rienhoff announced that apparently it was not necessary to obliterate this space by thoracoplasty, my own ideas wavered considerably, and after doing several total pneumonectomies without the performance of thoracoplasty, I decided that probably Dr Rienhoff was right. Since that time, however, my own mind has wavered a good deal back and forth.

I think that we thoracic surgeons ought to be very grateful to Dr Cournand and Dr Berry for these very fine studies which have been reported here this morning. These in a sense, also tend to confirm observations that were reported before the Association of Thoracic Surgery by Longacre two years ago, in which, also, evidence was brought out that probably in the long run the patient who has had a pneumonectomy would fare better if he had the space completely obliterated by thoracoplasty.

Now, if however one attempted to add a thoracoplasty as an initial procedure to the operation of total pneumonectomy, in all probability the mortality of the operation would rise. In the early days, I undertook to compromise this measure somewhat by performing a thoracoplasty first, in some cases, followed by total pneumonectomy. That procedure I abandoned because for various reasons I do not think it is a wise one.

In the patients whom Dr Berry recorded as carrying a permanent pneumothorax substituted by an oleothorax, that perhaps is an effective measure which might be satisfactory in patients who might otherwise be a poor risk for subsequent thoracoplasty. But after all, of course carrying a lot of oil around in the chest is carrying a foreign body and oleothorax for tuberculosis has had a rather high proportion of unsatisfactory results largely because it is a foreign body that is carried around.

Dr Rienhoff, however, suggested some years ago, that it is not necessary that a thoracoplasty be performed at the time of the operation. If it should seem necessary it can be done some time later, and I think that that is sound advice.

DR FRANK B BERRY (closing) I should like to thank Dr Graham very much for his kindly discussion, and say that I agree completely with him about the dangers of oleothorax, and it was merely given to D M as a makeshift as we still hesitate to undertake a thoracoplasty on him.

We have had two other patients lately in whom this question has arisen. One was the man for whom we did a pneumonectomy for intrabronchial tuberculosis. He has been hospitalized since 1924. That is a great handicap to overcome. Following his pneumonectomy, he still had many aches and pains. His chief complaint was difficulty

in swallowing though we could not demonstrate anything by esophagograms. We finally suggested that perhaps it was due to distention of his other lung and some push or pull which we could not demonstrate. Following thoracoplasty, he has been completely relieved, notwithstanding relatively good functional studies all along. He is now inquiring about the chances of getting a job, so apparently from the purely subjective standpoint it was completely worth while.

Another is a man of sixty. Following his pneumonectomy, he decided the best way to put himself in shape was to forget all about hospitals and promptly built himself up to the ability to walk ten miles a day. Two years later this winter, he came back to us with pneumonia from which he recovered and again he left the hospital. He came back a few weeks later with acute dyspnea and was markedly cyanotic from a diffuse bronchitis. Since then during his convalescence he has had similar attacks—paroxysms with acute dyspnea. I became very much worried about the possibility of his overdistention and within the last week we put him through complete studies only to find that at the end of two years his lung still is about in the midline, there is a very good diaphragmatic excursion, oxygen saturation of 95 per cent and exceedingly good maximum breathing capacity. So we have decided that his trouble is due probably to a true bacterial asthma coming on in paroxysms and has nothing to do with overdistention of the remaining lung.

Now we have never undertaken a thoracoplasty on him nor do we intend to as long as he maintains this position which it seems likely he will and he has filled the operated side of his chest just as Dr. Rienhoff has suggested, with some sort of plug of fibrin and coagulated serum sufficient to hold his mediastinum in place. In view of these recent difficulties we were very much astonished to find such very good functional response in the midst of these series of paroxysms.

A PRACTICAL CONSIDERATION OF OPEN PNEUMOTHORAX UNDER SODIUM EVIPAL, SODIUM PENTOTHAL, AND ETHER ANESTHESIA*

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THE CHANGES in breathing which are induced by the collapse of the lungs were first described comprehensively by Hering and Breuer⁶ and by Head⁵. Although the experiments that they performed were carried out upon rabbits, the alterations they observed in the character of respiration are similar to the changes in breathing that occur when open pneumothorax is induced in dogs and human beings. The alterations in the character of breathing are as follows. An initial dominance of inspiratory activity and a retardation of breathing, a subsequent equalization of inspiration and expiration and an acceleration of the rate, and, finally, in many instances, the dominance of the expiration and a slowing of the rate. The initial dominance of the inspiratory act is probably the result of the changes in vagal reflex activity that are brought about by the collapse of the lungs³. The subsequent changes in breathing that occur as the period of pneumothorax extends are dependent, to a large extent, upon the development of asphyxia^{1, 4}.

In view of the number of penetrating wounds of the chest that are now being suffered, a study of the effects of anesthetic agents upon the respiratory phenomena that are associated with open pneumothorax seemed to be justified, especially since a definite possibility exists that the knowledge gained from the experiments could be employed in treating people who suffer chest injuries.

METHODS

The general equipment and procedures have been described previously¹.

Pneumothorax was instituted by opening the side arm of a flanged cannula of $\frac{3}{4}$ -inch bore. The cannula was inserted into the right chest through the periosteal bed of the fourth or fifth rib. The mediastinal pleurae were perforated, therefore, the opening of the cannula permitted the lungs to collapse quickly. The withdrawal of air through the side arm reexpanded the lungs. Ninety-five per cent alcohol was injected into the intercostal nerves that were available in the field of operation. This was done in order to prevent nociceptive stimuli, set up by the retention of the cannula in the chest wall, from modifying the breathing.

The animals were anesthetized with sodium evipal† (1 methyl 5 Δ' cyclohexenyl 5 methyl barbiturate) 50 mg per kilogram, sodium pentothal†

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942.

† Evipal and pentothal are used throughout the remainder of the paper to designate the sodium salts of these barbiturates.

(ethyl (1-methylbutyl) thiobarbiturate) 25 mg per kilogram, or "open drop" ether. During the preparation of the animals for the experiments, the anesthesia was maintained at moderately deep levels. Before the experi-

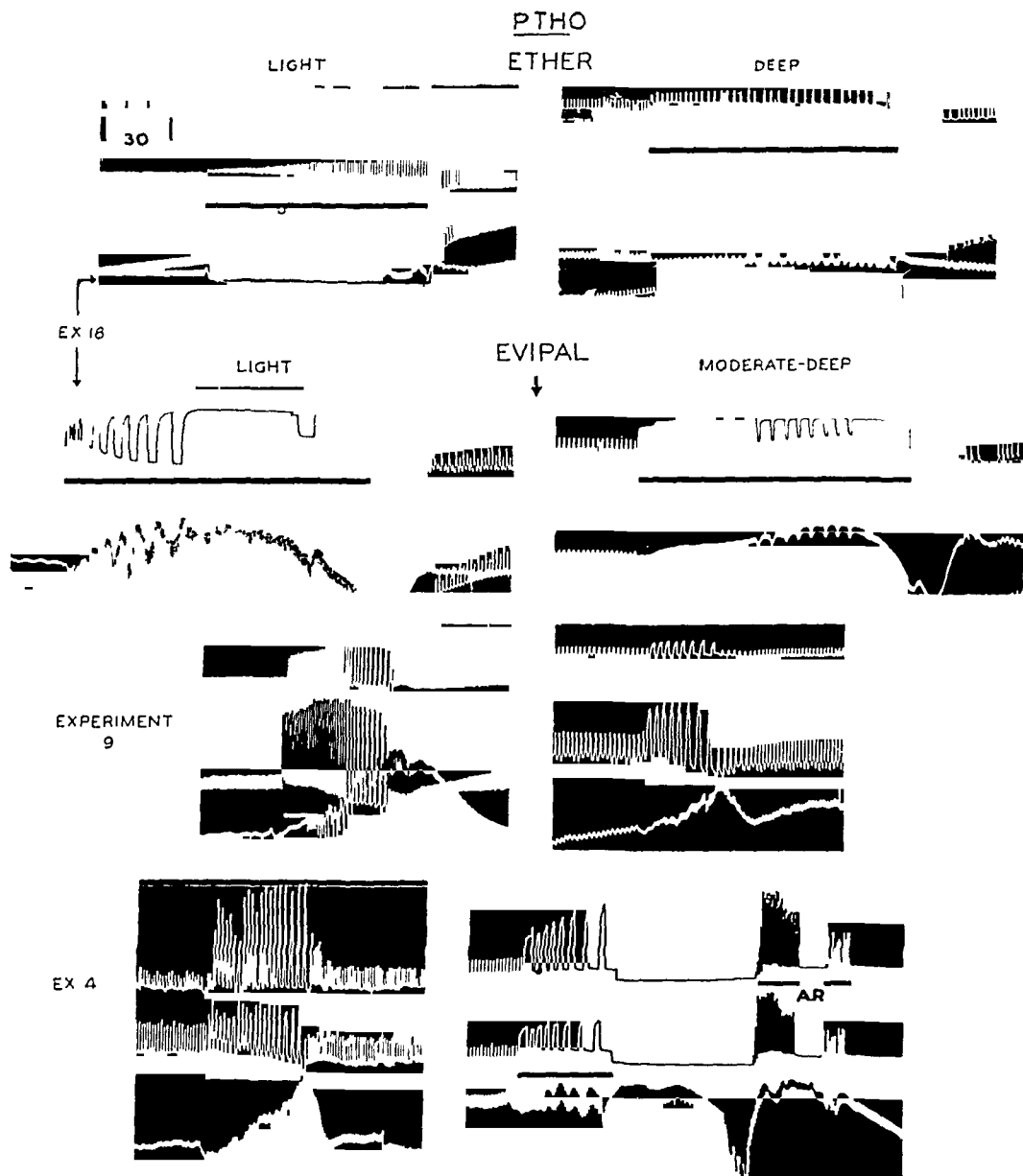


Fig 1—Illustrates the responses to open pneumothorax under light and deep anesthesia. Experiment 18 was begun with ether anesthesia and terminated with evipal anesthesia. Experiments 9 and 4 were conducted under evipal anesthesia.

mental procedures were begun, the anesthesia was regulated so that the corneal, the lid, and the patellar reflexes were very active, and the electrically excited, reflex contraction of the semitendinosus muscle relaxed slowly.

Three respiratory tracings were obtained. Tidal air (spirometer)*, chest breathing, and abdominal breathing. An inspiration was recorded as an

*The spirometer and chest tracings have been omitted in many of the illustrations in order to conserve space.

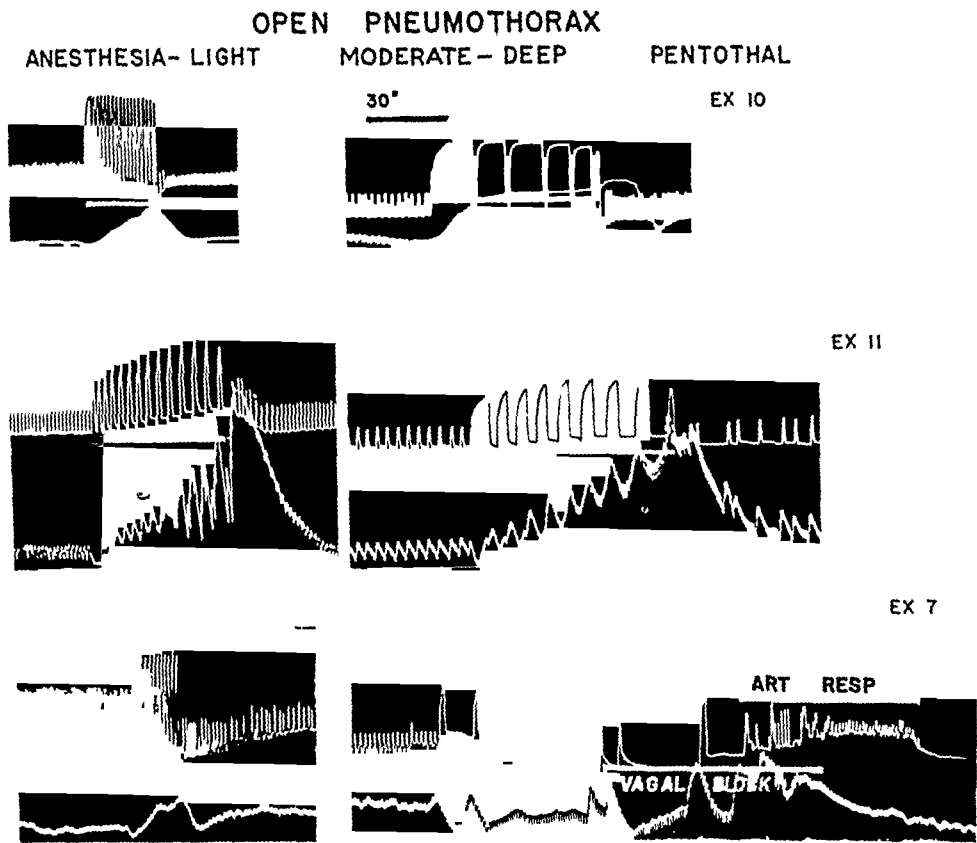


FIG 2—Illustrates the respiratory responses to open pneumothorax under light and deep pentothal anesthesia

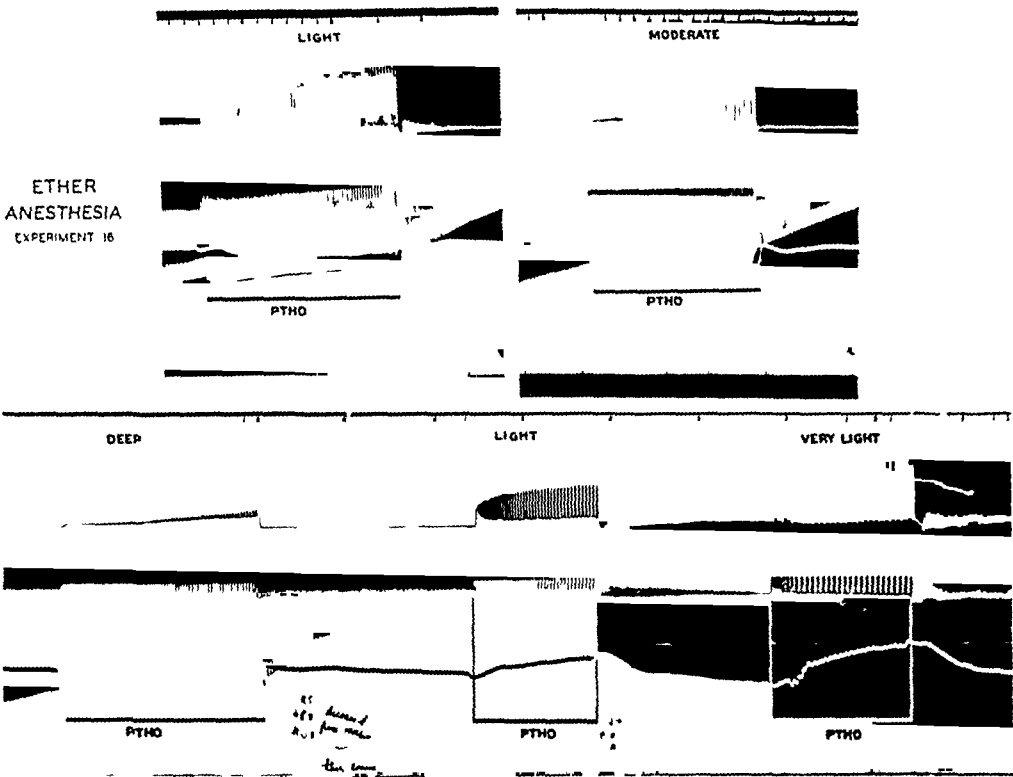


FIG 3—Illustrates the respiratory responses to open pneumothorax under light, moderate, and deep ether anesthesia. The rapidity with which the respiratory reactions change when the ether anesthesia is discontinued is shown in the lower record within five minutes the response changes from that labeled "deep" to that labeled "very light"

upstroke on all of the records. A mercury manometer was used in recording the mean blood pressure in the femoral artery or in the carotid artery.

RESULTS

Twenty experiments were performed. Seven with evipal anesthesia, eight with pentothal anesthesia, and five with ether anesthesia. The types of the respiratory responses to open pneumothorax are illustrated in the first three figures (Fig 1—evipal, Fig 2—pentothal, Figs 1 and 3—ether). During light pentothal, evipal or ether anesthesia the reactions of the animals to collapse of the lungs were similar. First, inspiration was intensified and prolonged. After the first respiratory cycle during pneumothorax had been completed, the prolongation of the inspiratory phase decreased and the intensity of the expiratory phase increased. These changes were associated with an increase in the rate of breathing. In many experiments the duration of expiration subsequently increased gradually and the respiration decreased in rate (Fig 1, Fig 2—Experi 11, and Fig 3). After the lungs were reexpanded a rate of breathing that was slower than the antecedent normal rate was present for varied periods of time.

During moderately deep anesthesia open pneumothorax produced varied changes in the character of breathing. When evipal or pentothal were employed as anesthetics, three distinct types of reaction to the collapse of the lungs were apparent. One is characterized by a relative inspiratory apnea (Experi 18, Fig 1 (evipal), and Experi 10, Fig 2), another by a fairly equal prolongation of the inspiratory and expiratory acts (Experi 9, Fig 1, and Experi 11, Fig 2); and the last, by a relative expiratory apnea (Experi 4, Fig 1, and Experi 7, Fig 2). The type distribution of the experiments done with evipal and pentothal anesthesia is shown in Table I.

The institution of open pneumothorax during moderately deep ether anesthesia was followed by qualitatively similar reactions in all of the animals, the intensification and prolongation of the inspiratory phase is less, and the prolongation of the expiratory phase is greater than the respective reactions were when the anesthesia was light (Figs 1 and 3).

The responses to reinflation of the lungs (the termination of the period of pneumothorax) were also variable when moderate to deep evipal or pentothal anesthesia was employed. In general the animals placed in Group I (Table I) breathed more rapidly and more deeply, and those placed in Group II breathed more slowly and more deeply after the period of pneumothorax than they did before it. The animals in Group III were apneic after the lungs were reexpanded. Of the seven animals in Group III, three (two that were anesthetized with pentothal and one with evipal) failed to breathe spontaneously after a brief period of lung collapse (30 seconds or less). Their breathing was eupneic before the pneumothorax was instituted. Intermittant artificial respiration was performed on these animals for 33 to 56 minutes. This maneuver succeeded in maintaining the mean blood pressure

of the animals above 130 Mm as long as it was performed. However, an adequate spontaneous respiration was not reestablished. The other four animals in Group III recovered after the performance of artificial respiration or after the intratracheal administration of oxygen. Varied mechanisms are involved in the production and maintenance of the long postpneumothorax

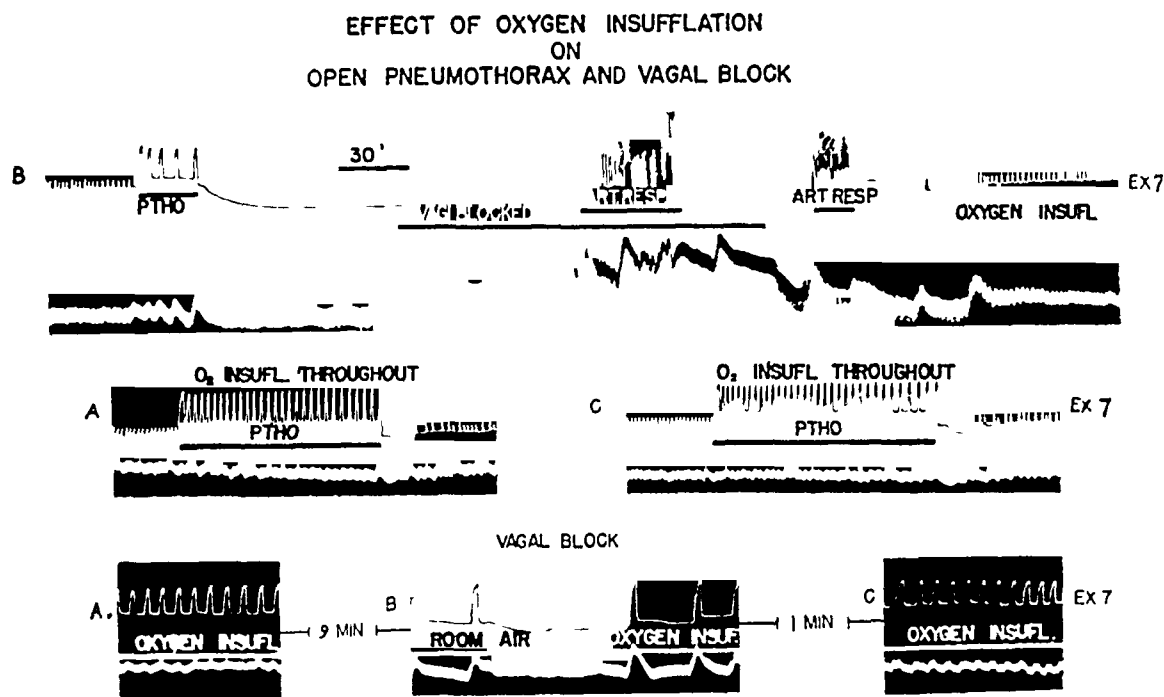


FIG. 4.—Illustrates the effect of the oxygen insufflation upon respiration during and after open pneumothorax, and upon respiration during bilateral cervical vagal cold block.

apneas. Asphyxia plays a very important rôle. If the asphyxia that frequently exists during moderately deep barbiturate anesthesia¹ is relieved and the development of the asphyxia that follows the collapse of the lungs is delayed or entirely stayed, by the intratracheal insufflation of air or oxygen, the long apneas do not occur (Fig. 4). The record A was obtained after

TABLE I

Anesthesia	Total Number of Animals	Group I Relative Inspiratory Apnea	Group II Balanced Breathing	Group III Relative Expiratory Apnea
Moderate—Deep				
Sodium evipal	7	1	3	3
Sodium pentothal	8	2	2	4

the postpneumothorax apnea, illustrated in Fig. 2, Exper. 7, was broken by the intratracheal insufflation of oxygen. This oxygen insufflation was continued through A of Fig. 4. (Compare A of Fig. 4 with Exper. 7 of Fig. 2, and B of Fig. 4). Note the relative absence of expiratory dominance during the longer period of pneumothorax and the relative brevity of the postpneumothorax apnea when pneumothorax is instituted and stopped while oxygen is being insufflated, as compared with the response of the same animal when air is breathed before the pneumothorax and the insufflation of oxygen is not employed. Note in Figure 4 B that the long expiratory

postpneumothorax apnea was not successfully broken by artificial respiration but that it was very quickly relieved with the insufflation of oxygen. Part C of Figure 4 followed B and the result is practically identical with that previously obtained under similar experimental conditions—Part A.

Although asphyxia produced great changes in breathing during and after

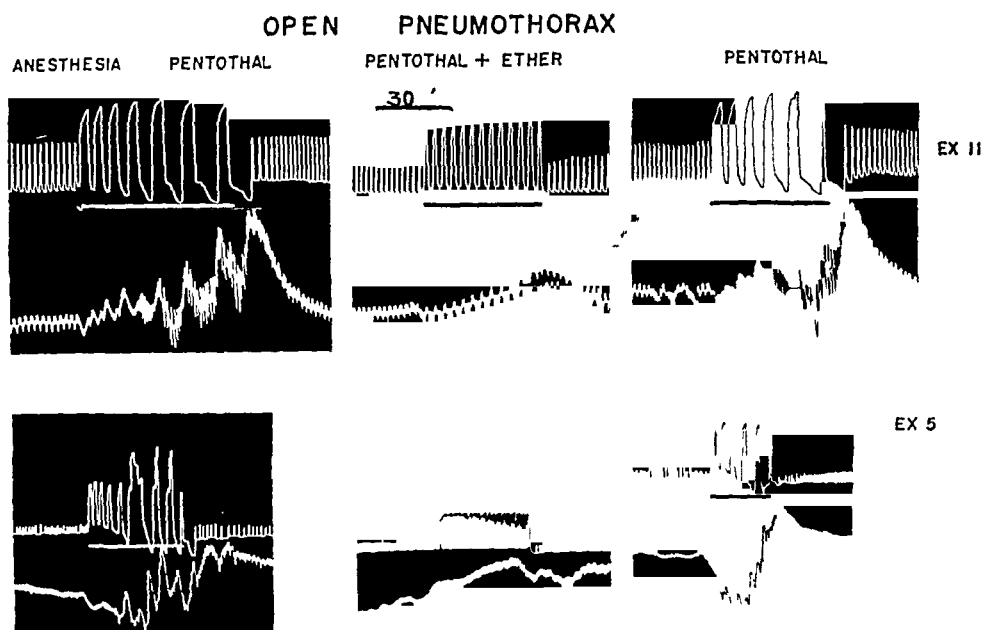


FIG 5—Illustrates the effect of ether upon the respiratory response to open pneumothorax under moderate pentothal anesthesia.

pneumothorax when evipal and pentothal are employed as anesthetics it does not produce similar changes in breathing when ether is used (Fig 1, Exper 18—ether, and Fig 3). Not only is this apparent when the barbiturate and ether series are compared, but it is also seen in single experiments. The section of Figure 1, Exper 18, that is labeled ether anesthesia, shows the respiratory reactions to pneumothorax under light and deep ether anesthesia, the section labeled evipal, immediately below it, shows the responses of the same animal to pneumothorax after evipal has been substituted for the ether (ether discontinued and evipal given when the ether anesthesia became too light). It is obvious that there is little similarity between the reactions during ether and evipal anesthesia.

Expiratory dominance during pneumothorax (anesthesia—evipal and pentothal) is entirely suppressed by a little ether vapor. Compare the sections of Experiments 11 and 5, in Figure 5, labeled pentothal, with those labeled pentothal + ether. Ether vapor was administered to the animals for five and nine minutes, respectively, between the first and second records, and it was discontinued between the second and third. No pentothal was given between the first and the third records.

Experiment 6, Figure 6, demonstrates the respiratory stimulating action of ether. Before ether was administered to the animal which was moderately anesthetized with pentothal, life had been maintained for 37 minutes by arti-

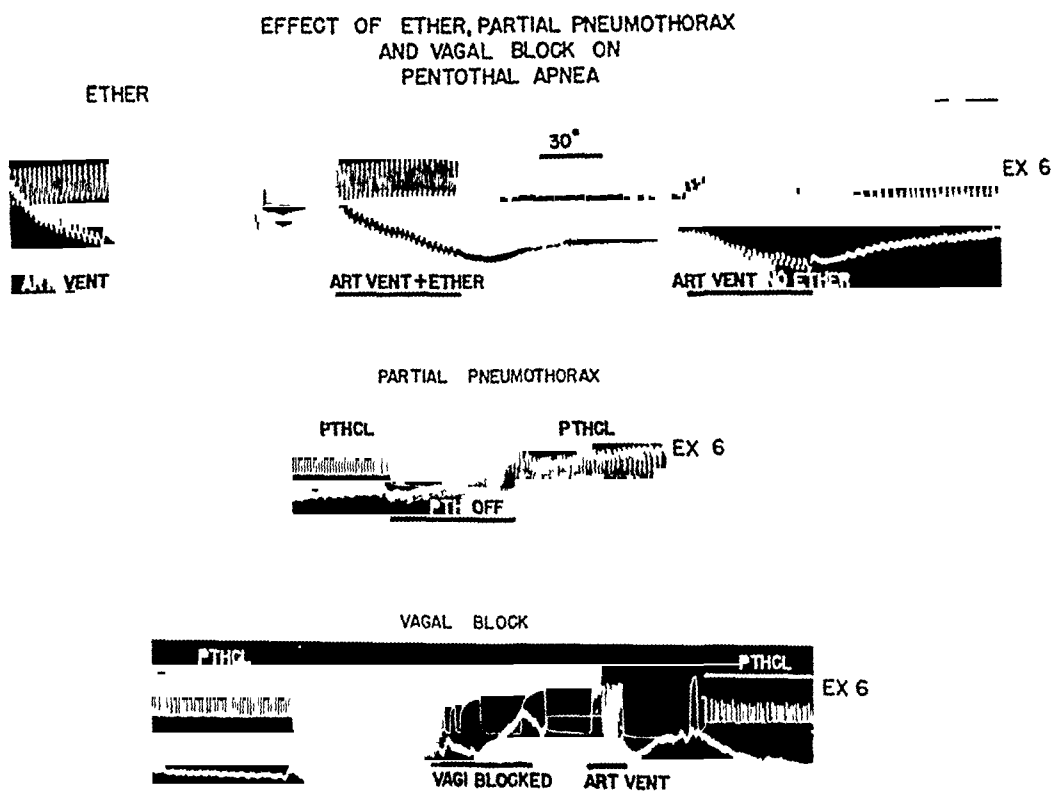


FIG 6—Illustrates the effects of ether, partial pneumothorax, and vagal block upon apnea that followed open pneumothorax under pentothal anesthesia

ficial respiration after breathing had stopped following a short period of open pneumothorax. The administrations of ether for one and one-half minutes during a period of artificial respiration resulted in eupneic breathing that gradually faded out as the ether was blown off, and breathing finally stopped again. See the period below labeled "pth—off."

DISCUSSION

The type of anesthetic and the depth of anesthesia effect great changes in the characteristics of the respiratory response to collapse of the lungs. It is not surprising that the primary inspiratory stimulating effect of pneumothorax is less when the animals are anesthetized with ether than it is when they are anesthetized with evipal or pentothal, for ether has a comparatively greater depressing action upon reflexes than these barbiturates have.² (The inspiratory stimulating action of lung collapse has a reflex origin).³

The development of either inspiratory (very rare) or of expiratory dominance (common) during pneumothorax in many of the experiments conducted at moderately deep levels of evipal or pentothal anesthesia and the development of expiratory dominance during pneumothorax in all of the experiments conducted at deep levels of ether anesthesia are probably the result of asphyxia, however, the mechanisms involved in their production appear to be different. The characteristics of the expiratory dominance under evipal or pentothal anesthesia indicate that it is due to a relative overactivity on the expiratory center. (Consult reference 3 for a detailed discussion).

Two of five animals when they were very lightly anesthetized with

ether, showed a small expiratory dominance of the overactive type (Fig 3). However, the characteristics of the expiratory dominance that develops during the period of pneumothorax when the animals are deeply anesthetized with ether, indicate that this dominance probably is due to the depression of breathing by asphyxia rather than to a selective stimulation of the respiratory center. These characteristics are the gradual onset and the even increase, the paucity of evidence for an increased strength of expiration, the even and gradual recovery that follows reexpansion of the lungs, the absence of qualitative variations in the responses of different animals, and the striking similarity that the dominance bears to the respiratory depression effected by anoxia in animals deeply anesthetized with ether.²

The development of a strong expiratory dominance of the overactive type predisposes the animals to long apneas when the lungs are reexpanded. Apneas that are of sufficient length to necessitate the use of artificial respiration to maintain life did not occur in the experiments in which an inspiratory dominance (Exper 18, Fig 1—evipal, Exper 10, Fig 2), or a balanced breathing (Exper 9, Fig 1, Exper 11 Fig 2) obtained during the period of pneumothorax. Expiratory dominance of the depressive type (deep ether—Exper 18, Fig 1, and Exper 16, Fig 3) did not predispose to long apneas in this series of experiments. No apneas of sufficient length to necessitate the use of artificial respiration were encountered during ether anesthesia. However, long apneas can undoubtedly be induced in animals deeply anesthetized with ether if the period of pneumothorax is extended enough to effect an asphyxial depression of the center to such a degree that spontaneous recovery becomes improbable.

Many factors appear to be involved in the institution and the maintenance of the apneas that follow open pneumothorax. The withdrawal of the intrathoracic air, that terminates the period of pneumothorax, rapidly increases the volume of the lungs, this increase in volume stimulates expiration. If the Hering-Breuer reflexes are active, as they usually are, in animals anesthetized with evipal or pentothal, the expiratory stimulating effect of inflation of the lungs will tend to reinforce the expiratory dominance developed during the pneumothorax. Although this mechanism very likely plays some part in the institution of the apneas, it is not of primary importance because the postpneumothorax apneas occur when pneumothorax is instituted after the afferent pathways of the Hering-Breuer reflexes (the vagi) are blocked or cut.⁴ Furthermore, an overactivity type of expiratory apnea develops without the institution of pneumothorax when the vagi are blocked and asphyxia develops as the result of a decreased pulmonary exchange (Fig 4, bottom). Undoubtedly asphyxia is very important for the development and the maintenance of the apneas. If the onset of asphyxia during pneumothorax is stayed, the postpneumothorax apneas do not appear (Compare A and C with B or Figure 4). However, the effectiveness of asphyxia in producing the apneas is dependent upon the type of anesthetic and the depth of anesthesia. Very long apneas did not occur at any depth

of ether anesthesia or at light levels of evipal or pentothal anesthesia

Evipal and pentothal may effect either one or the other of two basic changes in the balance of the respiratory mechanisms that might account for the apneas either they increase the activity of the expiratory center more than that of the inspiratory center or they decrease the activity of the inspiratory center more than that of the expiratory center. The data provided by this series of experiments are inadequate to establish the validity of one or the other of the above possibilities, however, these experiments

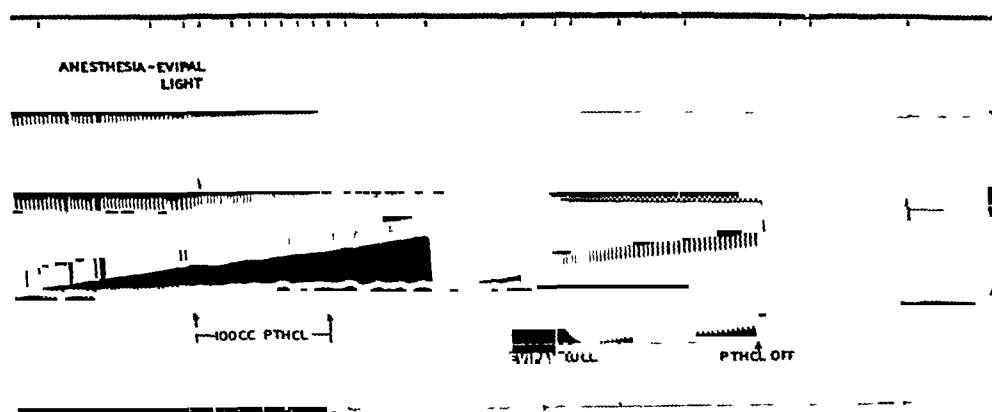


FIG 7—Illustrates the masking effect of a closed pneumothorax of 100 cc upon the respiratory depression effected by evipal and pentothal (This experiment was conducted under evipal anesthesia)

show that the apneas are easily broken by reflexly increasing inspiratory activity. The institution of the deflation Hering-Breuer reflex by admitting 150 cc of air into the chest (pthcl—closed pneumothorax) of an apneic animal institutes and maintains a eupneic breathing as shown in the beginning of the record in the middle of Figure 6. The withdrawal of the air (pth off) stopped breathing. Reinstitution of the closed pneumothorax (150 cc) reinstated breathing. The experiments demonstrate also that the administration of a small amount of ether to animals that are anesthetized with evipal or pentothal abolishes the expiratory dominance and breaks the apnea (Figs 5 and 6, respectively). These actions of ether might be due solely to its reflex depressant action. This possibility is very unlikely since a great dissimilarity exists between the effects of vagal block and ether. (Vagal block rapidly and completely suppresses the transmission of respiratory afferent stimuli of pulmonary and vascular origin that traverse the vagi). Compare the records at the top and bottom of Figure 6. Therefore, it is probable that the effectiveness of small amounts of ether in suppressing expiratory dominance and in breaking the apneas is due to its respiratory stimulating action. Ether has been proven to be a very effective respiratory stimulant in rabbits deeply anesthetized with the long-acting barbiturates⁷

Although the basic pharmacologic actions of evipal and pentothal which account for the disruption of breathing during and subsequent to pneumothorax have not been determined, it is apparent that the institution of a continuous inspiratory stimulation (closed pneumothorax), the administra-

tion of small amounts of ether, or the suppression of asphyxia (intratracheal insufflation of air or oxygen) will correct the disruption of respiratory balance

However, in spite of the fact that effective measures can be taken to prevent and to overcome the dangerous respiratory phenomena which occur during and after pneumothorax when evipal and pentothal are used as general anesthetic agents, these barbiturates should be considered as being more dangerous than ether. Consequently, they should be employed with utmost caution as general anesthetic agents, especially when pneumothorax exists or will be produced.

Besides the apparent dangers that confront the breathing under barbiturate anesthesia, there are other factors that make evipal and pentothal more dangerous than ether, even in the most skilled hands. The most important of these factors is the relative lack of definitive signs of anesthesia during evipal and pentothal anesthesia. There are only two governing signs for barbiturate anesthesia, namely, the anesthesia is deep enough when the surgeon operates without signs of painful stimulation appearing in the patient, and the anesthesia is too deep when respiration ceases. There are no reliable signs available during adequate anesthesia to permit the anesthetist to ascertain the imminence of respiratory arrest until it does occur. Furthermore, the limiting sign—the cessation of breathing—is exceedingly variable. Painful stimuli, anoxia, and inspiratory stimulating proprioceptive respiratory stimuli mask overdose.¹ The masking effect of a slight reduction in the volume of the lung is shown in Figure 7. Note that breathing increased when a 100 cc closed pneumothorax was produced, that the rate of breathing decreased from 38 to 18 cycles per minute after one cubic centimeter of evipal was given, and that after a steady breathing had been established, breathing stopped when the pneumothorax was terminated. The "premortal" asphyxial rise of blood pressure is seen at the extreme right—breathing was reinstated by a 100 cc pneumothorax, ten minutes later this was withdrawn and breathing stopped again. Forty-one minutes elapsed between the injection of evipal and the reestablishment of an adequate respiration without the stimulus of a small closed pneumothorax. Similar results were obtained in all of the experiments in which this procedure was performed (four with evipal, and three with pentothal). Therefore, the administration of evipal or pentothal, in the face of acute pneumothorax, must be done blindly and without assurance that breathing will continue after the operation is completed, the pneumothorax reduced, or the asphyxia, that is commonly associated with pneumothorax, is diminished.

In spite of the evidence that the barbiturates, in the presence of pneumothorax, are potentially more dangerous from the standpoint of breathing than ether, the experimental findings clearly indicate that pentothal could be safely and advantageously employed for the induction of ether anesthesia, especially in situations in which the gases ordinarily employed for this purpose are not available.

In circumstances that prohibit the use of ether, pentothal could be employed as a relatively safe anesthetic agent provided that the anesthetist and surgeon are cognizant of its limitations and the wide variations in breathing that frequently attend pentothal anesthesia.

Experiments recently performed indicate that hypercarbia (retention of carbon dioxide) rather than anoxia is the dominant component of asphyxia in the production of the disruptions in respiration that have been described. Therefore, increasing the oxygen content of the air inspired by the patient during the operation will not prevent these phenomena, because this expedient accelerates the development of hypercarbia when employed during pentothal anesthesia. The intratracheal insufflation of air or oxygen is the only measure that can be relied upon to prevent asphyxia or relieve it.

SUMMARY AND CONCLUSIONS

The respiratory responses associated with open pneumothorax in animals lightly anesthetized with evipal, pentothal, or ether were quantitatively similar. The responses of animals more deeply anesthetized with evipal and pentothal were varied, some were primarily inspiratory, some were balanced, others were primarily expiratory. The responses of animals more deeply anesthetized with ether were of the expiratory type. The inspiratory or expiratory dominance that is present or develops during pneumothorax in animals moderately anesthetized with evipal or pentothal is probably due to selective stimulation of the respective respiratory half centers and the expiratory dominance that develops during pneumothorax in animals deeply anesthetized with ether is probably due to depression of the center.

The presence of expiratory dominance during pneumothorax in animals anesthetized with evipal or pentothal predisposes to long postpneumothorax apneas. The development of expiratory dominance and of the postpneumothorax expiratory apneas is prevented by the intratracheal insufflation of air or oxygen or the administration of small amounts of ether.

The postpneumothorax apneas are broken by the intratracheal insufflation of air or oxygen, by a small amount of ether, or by a slight reduction in the volume of the lungs.

No postpneumothorax apneas were noted in animals that were anesthetized with ether.

A small closed pneumothorax masks the respiratory depressing action of evipal and pentothal.

Although, from a physiologic viewpoint, pentothal is less safe in the presence of pneumothorax than is ether, especially if asphyxia is present or develops, pentothal may be safely and advantageously employed to induce anesthesia that is to be maintained with ether, because ether effectively counteracts the untoward respiratory reactions seen under pentothal anesthesia.

BIBLIOGRAPHY

- ¹ Beecher, H. K., and Moyer, C. A. Mechanisms of Respiratory Failure under Barbiturate Anesthesia (Evipal, Pentothal). *J. Clin. Invest.*, 20, 549, 1941.

² Beecher, H K, and Moyer, C A Unpublished data

³ Gesell, R, and Moyer, C A Changes in the Balance of Respiratory Drives Resulting from Open Pneumothorax Am J Physiol, 135, 539, 1942

⁴ Gesell, R, Moyer, C A, and McKittrick, J Some Special Instances of Predominant Chemical Stimulation of the Expiratory Half-Center Am J Physiol, in press

⁵ Head, H Regulation of Respiration J Physiol, 10, 1, 1889

⁶ Hering, E, and Breuer, J Die Selbststeuerung d Athmung durch den Nervus Vagus Litzgsber, Akad Wiss, Wien, Math-natur wiss kl, 58, (2 Abt), 909, 1868

⁷ Klopstock, R Personal communication

DISCUSSION—DR J B MCKITTRICK (Ann Arbor, Mich) I would like to add a very brief word to what Dr Moyer has already told you It has to do with effects of high concentrations of oxygen and carbon dioxide in animals anesthetized with evipal and pentothal This is pertinent to the pneumothorax problem, and is also important in dealing with patients anesthetized with these anesthetic agents for other conditions

(Slide) These slides are set up exactly as those shown by Dr Moyer, the upper line representing the exchange of air as measured by spirometer, the second line showing costal respiration the third blood pressure and the lower line abdominal respiration Throughout this period represented by the base line 100 per cent oxygen is being administered this animal having been anesthetized with evipal During the administration of 100 per cent oxygen respiration gradually slowed down until finally it ceased entirely Various maneuvers were instituted to make these animals breathe again namely negative and positive pressure—that is intrapulmonary pressure *via* the spirometer and artificial respiration of the chest Neither of these was successful As soon as the 100 per cent oxygen was removed and the animal returned to room air practically normal respiratory action ensued

(Slide) If you will pay attention to this upper line and forget the rest here again is an animal anesthetized with evipal Sections A B and C represent increasing depth of anesthesia The animal is given 12 per cent carbon dioxide and 28 per cent oxygen Twenty-eight per cent oxygen functions to eliminate the stimulating factor of anoxia You can see as the anesthetic depth is increased, the respiration again becomes progressively slower and if the mixture is continued will eventually cease

It is only safe to inject a word of caution in using the common respiratory and resuscitative measures namely common dioxide and oxygen in patients who have ceased to breathe under these anesthetic agents

DR FREDERICK A COLLIER (Ann Arbor Mich) I simply wish to state that my connection with this paper is due entirely to my interest in it and the work was all done by Drs Moyer and McKittrick

I think the question might be raised whether at the present state of the practice of surgery a surgeon should any longer concern himself with these questions of anesthesia or leave them in the hands of the anesthesiologist My feeling is that there are as yet too few of them and that we still must concern ourselves with the subject of anesthesia because I find that when a patient dies under an anesthetic I am the person who has to tell the family so I still must take an interest in it

There is one point I would like to emphasize because it has seemed important and helpful to me and that is that painful stimuli mask the depth of the anesthesia induced with the modalities we have been discussing Last week we saw a most interesting case in a nearby town Sodium pentothal was used for a very difficult bronchoscopic examination and apparently there were difficulties to be overcome, and the anesthesia became deeper and deeper Finally the procedure was over the painful stimuli ceased and the patient ceased to breathe of course because of the lack of the painful stimulation incident to the bronchoscopic examination They gave the patient all the usual stimulants and I think several other things that happened to be on the shelf without avail Artificial respiration was then started and 30 minutes later the patient began to breathe Of course he was a decerebrate being from then on and still is due to this prolonged anoxia Had they known enough to have given him ether and oxygen as has been brought out in this paper with forced respiration the patient would have gone on to a successful convalescence

I know that all of us have given many patients sodium pentothal without danger I think however that we should know that many people do not have this good fortune The man who gave this particular anesthetic had only employed it six times previously Upon inquiry we found two other instances where amateur anesthetists had a death rate

of about one in one hundred, which is too high. The deaths could all be averted had they known the advice given to us this morning. There is much that we still have to learn about anesthesia, and I believe a surgeon should have an up to date knowledge of all that is known.

DISCUSSION—DR EDWARD D. CHURCHILL (Boston, Mass.) There is one sentence in Dr. Moyer's paper which probably was too informal to be carried into the published version. I should like to have it appear in the discussion, namely: "Despite the fact that these animals were under the most careful scrutiny with a constant record of blood pressure, pulse, respiration, and objective signs for the depth of anesthesia." Dr. Moyer said: "Before we knew what was happening we lost three animals under pentothal anesthesia."

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TRANSTHORACIC RESECTION OF TUMORS OF THE ESOPHAGUS AND STOMACH*

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PART II

ABBREVIATED CASE REPORTS OF THE OPERATIONS WHICH
FORMED THE BASIS FOR THE ARTICLE APPEARING IN THE
ANNALS OF SURGERY, Vol 15, No 6, 897-920, June, 1942

CASES OF CARCINOMA OF THE MIDTHORACIC ESOPHAGUS (ZONE II)

Case 1—M G H, No 162314 Female, age 43 Admitted 11/10/38 Epidermoid carcinoma, Grade III, at level of 7th dorsal vertebra Obstructive symptoms one year General nutrition good No demonstrable metastases

1/17/39—Jejunostomy Upper abdomen not examined

2/3/39—Transpleural esophagectomy (right side approach) Esophagus isolated in neck Resection 4th rib and division 5th Azygos vein divided Esophagus sectioned four inches above cardia and distal stump inverted Proximal esophagus and growth delivered through cervical incision

3/20/39—Celiotomy Esophageal stump delivered from mediastinum and brought to abdominal wall Left gastric artery preserved

4/20/39—Retracted lower stoma revised Upper stoma revised

7/19/39—First-stage skin-tube plastic

10/13/39—Second-stage skin tube plastic (Fig 3)

3/28/40—Third-stage skin tube plastic

Result Ingestion of semisolids and liquids Delay at lower stoma required "milking" contents of antethoracic esophagus into stomach Resumed activities as housewife on small farm

12/17/40—Small left pleural effusion

12/23/41—Bone metastases

2/7/42—Died with disseminated metastases

COMMENTS Prolonged jejunostomy and stomal feedings caused weakness of muscles of deglutition, so patient had to "learn to swallow" after tube completed

Lower stoma formed from esophagus produced delay in passage of food from tube to stomach

Death in three years, from metastases, despite favorable operative findings and complete operation

Case 2—M G H, No 179379 Female, age 63 Admitted 4/10/39 Epidermoid carcinoma, Grade III, at level of aortic arch Substernal pain two months No obstructive symptoms General condition good No demonstrable metastases

5/5/39—Jejunostomy without exploration

5/25/39—Transpleural esophagectomy (left side approach) Resection 5th rib Growth, adherent to vertebral column behind aorta, was broken into during dissection

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

Removed, with two-inch margin above and below Lower stump inverted Proximal esophagus delivered through left cervical incision An intercostal artery at aortic arch torn during dissection controlled by ligature Catheter drainage of chest

COMMENT Acute mediastinitis from rupture of growth at operation aborted by sulfonamide therapy Patient died 32 days after operation of hemorrhage from aortic point of origin of intercostal artery weakened by residual infection at former site of tumor

Case 3—M G H No 234193 Male, age 48 Admitted 2/5/40 Epidermoid carcinoma, Grade III, just below level of bifurcation of trachea Dysphagia five months No pain Fifty pounds weight, loss, emaciated, anemic Blood chemistry normal No obvious metastases

2/17/40—Jejunostomy without exploration Transfusion

3/27/40—Transpleural esophagectomy (right side approach) Resection 6th rib Division 7th rib Azygos and superior intercostal veins divided Esophagus divided well below growth and distal stump inverted Proximal esophagus and growth delivered through cervical incision Left pleura opened during dissection Closure impossible

4/15/40—Exteriorization of distal stump of esophagus, esophageal hiatus sutured, left gastric vessels and vasa brevia divided Biopsy of lymph node near left gastric vessels showed metastatic epidermoid carcinoma

Result Returned to work, ate liberal diet, using rubber tube connection Developed stenosis of lower esophageal stoma

1/15/41—Beck-Jianu gastrostomy Lower stoma showed recurrence of carcinoma in esophageal wall

6/6/41—Died, with metastases

COMMENT Use of esophagus distal to tumor in reconstructive procedure (1) invites disaster from inadequate removal of cancer, and (2) provides too small a stoma Cases 1 and 3 led to substitution of Beck-Jianu gastrostomy as more acceptable procedure

Case 4—M G H No 220533 Male, age 53 Admitted 7/2/40 Epidermoid carcinoma, Grade II, in lower third of esophagus Attacks of epigastric pain after eating No vomiting General condition and nutritional state good

7/24/40—Jejunostomy with exploration No abdominal metastases, left gastric nodes not involved

8/3/40—Transpleural esophagectomy (left side approach) Resection 8th rib Division ribs 7, 6, 5, 4 Growth not adherent Esophagus divided 1½ inches above cardia and distal stump inverted Right vagus nerve cut Proximal esophagus and growth delivered through cervical incision, growth removed, proximal esophagus brought down through subcutaneous channel and out below clavicle No drain

9/6/40—Beck-Jianu gastrostomy, long tube, left gastric vessels and two upper vasa brevia cut

Result Excellent functional result, using a rubber tube connection Gained 40 pounds

6/22/41—Metastases in upper mediastinal lymph nodes

9/7/41—Died with disseminated metastases

Case 5—M G H No 279893 Male, age 59 Admitted 12/11/40 Epidermoid carcinoma, Grade II, opposite aortic arch Obstructive symptoms several months, substernal pain while eating for three weeks Well nourished, good condition, no demonstrable metastases

12/23/40—Beck-Jianu gastrostomy No metastases to liver or subdiaphragmatic nodes

1/9/41—Transpleural esophagectomy (left side approach) Intercostal incision, 8th

interspace Posterior division of ribs 8, 7, and 6 Growth adherent to vertebral column, first upper right and two upper left intercostal arteries divided so as to retract aortic arch Both vagus nerves cut Lower esophageal stump inverted close to cardia, proximal esophagus and growth delivered through cervical incision, growth removed, proximal stoma brought out below clavicle

6/7/41—First-stage skin-tube plastic using skin along right side of chest to be transplanted later to left side Hairy chest

9/3/41—Second-stage skin-tube plastic

10/17/41—Third-stage skin-tube plastic

Result Developed pneumonia, finally showed evidence of recurrence Died 4/24/42 (Reported in Table II as a surviving case) Autopsy showed local recurrence in mediastinum with invasion of vertebral column

COMMENT Chest too hairy for use of skin between stomata Rope-graft tube constructed from right lateral chest in hairless area, completed and ready for transfer to left side Death from recurrence intervened before final stage was completed

Case 6—P M H No 40 1504 Admitted 9/30/40 Epidermoid carcinoma, Grade I, opposite aortic arch Dysphagia four months Poorly nourished, 30 pounds weight-loss No demonstrable metastases

10/15/40—Beck-Jianu gastrostomy No abdominal metastases found

11/4/40—Revision of gastrostomy, insertion of temporary rubber tube into lower end

11/14/40—Transpleural esophagectomy (left side approach) Resection of 7th rib Division of ribs 6, 5, and 4 Esophagus divided close to diaphragm, distal stump inverted Upper two intercostal arteries divided to allow retraction of aortic arch Proximal esophagus and growth delivered through cervical incision, growth removed, stoma established in neck because of high growth Catheter drainage of chest

12/23/40—Celiotomy Gastrostomy closed Distal esophageal stump pulled down Left gastric and left gastro-epiploic vessels divided, entire upper half of stomach brought up in a subcutaneous channel in anterior chest wall and lower esophageal end brought out through a small incision opposite nipple

4/14/41—First stage skin-tube plastic

6/5/41—Second-stage skin-tube plastic

7/30/41—Celiotomy Heineke-Mikulicz pyloroplasty to overcome persistent pylorospasm due to lack of vagus function and unopposed sympathetic action

8/30/41—Third-stage skin-tube plastic

Result Remains well Eats liberal diet of soft solid food No delay in antethoracic esophagus (See Figures 4 and 5 for photographs of completed external esophagus)

Case 7—P M H No 41 900 Admitted 6/8/41 Adenocarcinoma arising in aberrant gastric mucosa, lower portion of middle half of esophagus Dysphagia seven months Twenty-five pounds weight-loss General condition good

6/20/41—Transpleural esophagectomy (left side approach) Resection 8th rib, division of ribs 7, 6, 5, 4 Growth too high for esophagogastrostomy Esophagus divided at cardiac orifice Inversion by suture Proximal esophagus with growth delivered through cervical incision Both vagi cut because of adherence to growth Upper stoma brought out well below clavicle

6/28/41—Beck-Jianu gastrostomy Good swallowing ability by using rubber tube connection

9/10/41—First-stage skin-tube plastic Developed a virulent lobar pneumonia Sulfathiazole treatment failed

9/20/41—Died Autopsy showed no evidence of malignant disease

COMMENT No preliminary gastrostomy in this case because it was thought

before operation to be one for resection followed by an esophagogastric anastomosis. The plan of operation had to be changed when the growth was found, on exploration, to be too high to allow an anastomosis to be done.

Case 8—M G H No 37517 Male, age 72 Admitted 7/29/41 Epidermoid carcinoma, Grade III, opposite hilum of lung Dysphagia one month Ten pounds weight-loss General condition exceptionally good for age No demonstrable metastases

8/18/41—Beck-Jianu gastrostomy Long tube constructed Upper abdomen explored, no metastases found

9/8/41—Transpleural esophagectomy (left side approach) Resection 8th rib Division ribs 7, 6, and 5 Tumor not adherent Esophagus cut just above cardia, distal end inverted Proximal esophagus with growth delivered through cervical incision, growth removed, proximal stoma two inches below clavicle

Result Remains well Swallows with the aid of a rubber tube connection Refuses skin tube

COMMENT One of two small nonadherent growths, both patients are alive and well (Cases 6 and 8)

Case 9—P M H No 412016 Female 68 Admitted 12/11/41 Epidermoid carcinoma, Grade III, opposite 7th dorsal vertebra Dysphagia five months Marked emaciation and dehydration No obvious metastases

12/27/41—Beck-Jianu gastrostomy No metastases to liver or nodes below diaphragm Remarkable improvement in general condition

1/28/42—Transpleural esophagectomy Growth densely adherent to left main bronchus and aorta Posterior mediastinal vein torn, could not be secured without removal of esophagus Esophagus divided below growth, lower stump inverted Proximal esophagus delivered through cervical incision, growth removed, upper stoma below clavicle

Result Patient died on third day, cerebral thrombosis

COMMENT The accident of tearing a posterior mediastinal vein which could not be controlled without removing the growth forced completion of the operation Without this the operation would have been abandoned because of fixation of the growth

CASES OF TUMORS OF LOWER FOURTH OF ESOPHAGUS OR CARDIAC PORTION OF STOMACH (ZONE III)—TRANSTHORACIC APPROACH

Case 1—M G H No 212595 Male, age 59 Admitted 11/7/39 Adenocarcinoma, Grade II, involving cardiac portion of stomach and lower esophagus Progressive dysphagia two years Occasional hematemesis General condition excellent No anemia Growth seen by esophagoscope

11/12/39—Transthoracic partial gastrectomy with esophagogastric anastomosis Resection 9th rib Growth small No evidence of metastases End-to-side anastomosis, with silk Catheter drainage of chest Recovery uneventful

Result Remains well, works steadily No functional difficulty now, but noticed regurgitation first few months especially while in dorsal recumbent position

COMMENT An unusually favorable case with no lymph node or other metastases Good result could be anticipated

Case 2—M G H No 255165 Female, age 59 Admitted 6/15/40 Adenocarcinoma of the fundus of the stomach Anorexia three months Epigastric pain two weeks Anemic, emaciated Growth could not be seen through esophagoscope or gastroscope

7/17/40—Transthoracic partial gastrectomy Esophagogastric anastomosis, implan-

tation technic Intercoastal incision 8th interspace Growth large, lymph nodes around left gastric vessels involved, adherent, spleen removed with growth, phrenic nerve crushed Catheter drainage

Result Recovery complicated by empyema Died 11/8/40—bilateral pneumonia No autopsy

COMMENT This is the only case in the series where the unsatisfactory method of implanting the end of the esophagus through a hole in the stomach wall, without layer suture, was used Transitory leakage at the anastomosis was held responsible for the empyema

Case 3—P M H No 40 1549 Male, age 55 Admitted 10/8/40 Carcinoma of the fundus of the stomach involving the cardia Dysphagia six months Weight-loss, inanition, moderate anemia Two preliminary transfusions

10/15/40—Jejunostomy—Witzel method

10/25/40—Transthoracic partial gastrectomy, esophagogastric anastomosis Intercoastal incision, 9th interspace Division of 8th rib Phrenic nerve crushed Tumor large and adherent Many lymph nodes involved Careful layer suture, end-to-side, with silk No drain Uneventful recovery

Result Excellent immediate improvement No swallowing difficulty Gained weight One year later, October, 1941, began to lose appetite, weight, and strength Died two months later Autopsy revealed extensive metastases to liver and abdomen, local recurrence as well

COMMENT Good palliation of one year's duration, size and fixation of growth plus lymph node metastases made cure improbable

Case 4—M G H No 270238 Male, age 40 Admitted 10/23/40 Carcinoma of entire upper two-thirds of stomach Vomiting, anorexia, weight-loss, three months' duration Emaciation, anemia Gastroscopy failed to visualize tumor Peritoneoscopy showed no metastases

11/9/40—Transthoracic upper abdominal exploration Large carcinoma invading retroperitoneal tissues, firmly fixed, inoperable

Recovery uncomplicated Discharged in two weeks Died at home

Case 5—M G H No 273238 Male, age 68 Admitted 10/28/40 Adenocarcinoma of the cardiac portion of the stomach Fatigue one year Massive hematemesis, three weeks Marked anemia, serum protein 49%, poor general condition Polypoid growth seen by esophagoscope and gastroscope Peritoneoscopy No metastases seen Transfused several times

11/29/40—Transthoracic partial gastrectomy, esophagogastrostomy Resection 9th rib Large tumor, not adherent, nodes negative End-to-side layer suture with silk No drain Phrenic nerve crushed

12/17/40—Resection 6th rib left side for drainage of postoperative empyema No fistula Culture *Staphylococcus aureus* and nonhemolytic streptococcus

Result Empyema healed promptly Patient remains well Swallows without difficulty Roentgenograms show slight delay at pylorus

COMMENT One of three cases complicated by empyema

Case 6—M G H No 279061 Female, age 50 Admitted 11/27/40 Spindle cell sarcoma, fundus of stomach One and one-half years of recurring hematemesis, fatigue, loss of strength Mild anemia Condition good Tumor readily visualized through gastroscope

12/11/40—Transthoracic excision of the tumor Resection 9th rib Phrenic nerve crushed Tumor size of fist, in fundus Local excision performed—fundusectomy Silk

Result Recovery uncomplicated Alive and well

COMMENT One of two cases of relatively benign tumors of the fibroma-

sarcoma group removed by local excision

Case 7—P M H No 40 1862 Male, age 62 Admitted 11/27/40 Adenocarcinoma of cardia and fundus Infrascapular pain, anorexia, loss of weight, for two months Emaciated, anemic Peritoneoscopy showed the tumor, no metastases obvious

12/18/40—Exploratory thoracoceliotomy Resection 9th rib Small amount of fluid in chest Growth involved entire upper half of stomach and part of esophagus, firmly fixed posteriorly, many involved nodes, no other metastases Deemed inoperable, chest closed No drain

Result Prompt healing of wound Patient discharged at end of three weeks to nursing home, where he subsequently died of his disease

Case 8—P M H No 41 100 Male, age 72 Admitted 1/22/41 Negative exploration History of attacks of hiccough, epigastric distress and "dyspepsia" Well nourished, rather poor surgical risk Roentgenograms showed apparent carcinoma at cardia Esophagoscopy and gastroscopic examinations equivocal

2/1/41—Transthoracic exploration of upper abdomen No evidence of tumor or any other disease found

Result Recovery complicated by an attack of pulmonary edema Discharged 15th day Is living and well

COMMENT Esophagoscopy and gastroscopic examinations were inconclusive Too much reliance was placed on two roentgenologic examinations, both of which were thought to show carcinoma

Case 9—M G H No 94953 Female, age 67 Admitted 1/28/41 Epidermoid carcinoma, Grade III, of lower esophagus just above cardia Dysphagia, 4-5 months, anorexia, weight loss Emaciated, arteriosclerotic No demonstrable evidence of metastases

2/18/41—Transthoracic resection of lower esophagus and cardiac portion of stomach Resection 9th rib Lung very adherent, growth movable End-to-side esophagogastric anastomosis, silk Catheter drainage of chest

Result Recovery complicated by acute parotitis, otherwise normal Good function of stoma No stenosis (x-ray) Remains well, with no suggestions of recurrence

COMMENT Because of patient's age and history of carcinoma of sigmoid, resected in 1929, small margins of normal tissue above and below growth were allowed so as to make an anastomosis possible

Case 10—M G H No 294086 Admitted 3/21/41 Carcinoma of stomach invading lower esophagus Gradually increasing dysphagia and weakness, one year Anemic and poorly nourished

4/2/41—Transthoracic total gastrectomy, splenectomy, and partial pancreatectomy Resection 10th rib Phrenic nerve crushed No evidence of metastases Growth large, involved almost entire stomach including abdominal esophagus, fixation to spleen and pancreas Resection through lower esophagus and duodenum, spleen and tip of pancreas removed *en bloc* with stomach and adjacent lymph nodes Duodenum inverted easily End-to-side anastomosis of esophagus to upper jejunal loop, silk, two layers, jejunum suspended to crura of diaphragm, entero-enterostomy between two arms of jejunal loop Catheter drainage of chest

Result Developed empyema and acute pericarditis Autopsy revealed evidence of leakage at suture line

COMMENT The anastomosis was completed under too great tension

Case 11—M G H No 226834 Male, age 49 Admitted 4/24/41 Carcinoma of the cardiac portion of stomach involving the lower esophagus Postprandial substernal pain, six months Thin, emaciated No demonstrable metastases Esophagoscopy and gastroscopy revealed no evidence of tumor

5/2/41—Jejunostomy for feeding Upper abdomen explored No metastases except to lymph nodes Tumor surrounded cardia and involved abdominal portion of esophagus, extending to antium on lesser curvature

5/13/41—Transthoracic partial gastrectomy Resection of 9th rib, division of 8th rib Phrenic nerve crushed Growth adherent to base of transverse mesocolon, part of which was excised Large segment of stomach removed leaving greater curvature long Esophagus divided 1 inch above level of diaphragm End-to-side esophagogastric anastomosis, three layers, silk Catheter drainage of chest

Result Uncomplicated convalescence Functional result good No stricture (x ray) Transitory delay at pylorus lasting a few weeks Remains alive and well

Case 12—M G H No 300779 Male, age 43 Admitted 5/21/41 Carcinoma of stomach (signet-ring type) involving lower esophagus and lesser curvature to pylorus Epigastric pain ten months Anorexia five weeks General condition and state of nutrition good No anemia Growth seen by gastroscopy

6/10/41—First stage of two-stage transthoracic gastrectomy Proximal jejunal loop transected, end of distal portion inverted, proximal end anastomosed to the distal portion 12 inches below inverted end which was pushed into the lesser omental sac behind the stomach through an opening at the base of the transverse mesocolon Catheter jejunostomy below anastomosis

6/25/41—Transthoracic approach to stomach Growth found too extensive to remove Jejunal stump very adherent, tumor found in its mesentery Operation abandoned

Result Uneventful recovery Patient discharged home on 14th day

Case 13—P M H No 41 1050 Male, age 52 Admitted 6/26/41 Carcinoma of cardiac portion of stomach invading lower esophagus Pain in left lower chest, two years Occasional hematemesis, one year Thin but in reasonably good condition No demonstrable metastases

7/7/41—Transthoracic subtotal gastrectomy Resection 9th rib Left chest negative Phrenic nerve crushed Growth not adherent Esophagus sectioned 2½ inches above cardia Stomach cut obliquely, removing lesser curvature but leaving greater curvature End-to-side esophagogastric anastomosis, three layers, silk Five grams sulfanilamide inserted in upper abdomen and five in left pleural cavity No drain

Result Immediate recovery excellent Next day developed auricular flutter which failed to respond to treatment, developed pulmonary and cerebral edema, died third day after operation

COMMENT No lymph nodes on specimen showed disease

Case 14—M G H No 318650 Male, age 44 Admitted 8/29/41 Adenocarcinoma of lower esophagus and cardiac orifice, Grade III Substernal distress after deglutition, three months Good state of nutrition No demonstrable metastases

9/17/41—Transthoracic resection of lower esophagus and cardia Resection 9th rib Phrenic nerve crushed Esophagus divided two inches above growth, pathologist found tumor in cut edge, new level opposite inferior pulmonary vein chosen Stomach cut across obliquely well below cardia, lymph nodes near left gastric artery removed End-to-side esophagogastric anastomosis, two layers, silk Four grams of sulfanilamide left near suture line Catheter drainage of chest

Result Good early recovery No leakage of suture line, excellent function with no stenosis Developed small encapsulated empyema

10/15/41—Rib resection for drainage of empyema Uneventful recovery Wounds healed Remains well Working

COMMENT This case illustrates the fact that there is often considerable growth of tumor in the submucosal and muscular coats of the esophageal wall and serves to emphasize the necessity for allowing a wide margin of

apparently normal tissue beyond the obvious edge of the tumor (See also Case 3 of the Zone II series—midesophagus—where there was a recurrence of disease in the lower esophageal stoma)

Case 15—M G H No 319590 Male, age 54 Admitted 9/4/41 Adenocarcinoma of lesser curvature and cardia invading lower esophagus, Grade III Regurgitation of food, three months Marked loss of weight General condition fair, nutritional state depleted

9/12/41—Transthoracic partial gastrectomy and splenectomy Resection 10th rib Phrenic nerve crushed No metastases in chest or abdomen except lymph nodes near the growth which was large and adherent to the spleen *En bloc* removal of spleen with upper half of stomach and lower two inches of esophagus End-to-side esophago-gastric anastomosis, two layers, silk Four grams of sulfanilamide in chest Catheter drainage

Result Good recovery Uneventful convalescence No complications Function of anastomosis excellent, no stenosis (x-ray) Remains well

RECENT EXPERIENCES WITH THROMBOPHLEBITIS OF THE LOWER EXTREMITY AND PULMONARY EMBOLISM*

THE VALUE OF VENOGRAPHY AS A DIAGNOSTIC AID

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A STUDY OF STATISTICAL DATA in the recent literature on thrombophlebitis and pulmonary embolism shows (1) that approximately one of every 17 to 20 persons with clinically recognizable thrombophlebitis of the deep veins of the lower extremity will die of embolism, and (2) that one person of every 6 to 12 who have survived one or more attacks of embolism will die of a subsequent embolus,^{1, 2, 3} Since the great majority of pulmonary emboli, except those of cardiac origin, have been shown to arise in the deep veins of the lower extremity,^{4, 5, 6, 7, 8} a direct attack upon the site of origin is possible

The use of heparin has certain obvious disadvantages. Since there are no reliable earmarks by which to identify individuals susceptible to thrombosis, the routine use of heparin for successful prophylaxis against thrombosis would make the trouble and expense involved prohibitive. Its use for prophylaxis against embolism in patients with recognizable thrombosis or with evidence of nonfatal embolism may have real value. But heparin will not dissolve a thrombus, so that when it is discontinued, a propagating clot may form at the site of the thrombus or a new thrombus may form (Cases 2 and 10, *vide infra*). There is no way of knowing when it may be discontinued safely. Bleeding or hematoma formation at the site of operation and elsewhere may result from its use.

Other effective technics are, therefore, urgently called for. Homans and, after him, several others^{9, 10, 11, 12} divided the femoral vein as a prophylactic measure against embolism in isolated instances of thrombophlebitis of the lower leg. This procedure has not acquired the vogue which we believe it deserves. In a first series of patients so treated, we observed, in agreement with Homans, that (1) embolism did not occur, and (2) the phlebotic process in the leg subsided—in some instances at a remarkable rate. Pain decreased or disappeared in a day or two, and edema, when present, frequently began to subside more quickly than might be expected. The result was quite analogous to that obtained by novocain block of the paravertebral sympathetic trunk,¹² and was presumed to be due to a similar mechanism, *i e*, the breaking of a reflex arc producing vasospasm, with its undesirable sequelae.

Our experience with a second group of patients, who were studied with the aid of the venographic technic of Bauer,¹³ is the subject of this report.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

VENOGRAPHY

The deep veins of the lower leg are readily filled by the slow injection, with a fine needle, of 20 cc of a 35 per cent solution of diodast¹ into the small subcutaneous vein constantly present on the lateral aspect of the ankle. Any good vein on the dorsum of the foot may serve if the superficial veins of the leg are partially occluded by a blood pressure cuff. The foot is elevated on a six-inch block, and an anteroposterior roentgenogram is taken at the termination of the injection (60 seconds), with the foot rotated



FIG 1—Case 1. The arrow indicates a probable minor filling defect, which, together with signs of deep phlebitis, led to division of the femoral vein.

internally to expose the widest space between the fibula and tibia. The deep veins of the lower leg and the lower third or half of the femoral vein will be visualized on a 14 x 17 film. Increasing experience has taught us the importance of visualizing the entire femoral vein, so that we now utilize a larger film. The pattern of the deep veins varies considerably in different individuals, but, in general, there are two main trunks joining to form the popliteal, which continues as the femoral into the groin (Fig 11).

* We are grateful to the Winthrop Chemical Co for a generous supply of this material.

A varying number of branches of the superficial system, including the perforators, also appear, and they are of much narrower diameter than the deep veins. Since thrombosis is frequently present in an apparently uninvolved side, bilateral venography is generally indicated.

Filling defects in veins are of two types. Those due to venospasm alone, and those due to partial or complete occlusion by thrombosis or clot. Presumably the two may coexist, but we have recently obtained evidence, to be presented elsewhere, that a uniform narrowing or a complete absence of filling of part or the whole of one or more venous trunks can be due to pure venospasm. A reliable differentiation between the two processes awaits the development of an effective and simple technic to relax venospasm during roentgenography, so that the diagnosis of thrombophlebitis will be possible on the basis of structural filling defects only. Until such a method becomes available, we believe it wise to regard all filling defects as evidence of thrombophlebitis if infarction has occurred or if the signs and symptoms are suggestive. The venographic evidence of thrombophlebitis presented in this paper should, therefore, be interpreted in the light of these considerations.

When deep phlebitis is present, the small vein at the ankle will be tense and distended if the phlebitic process is at all developed. Resistance to flow will then be encountered, and a varying degree of absence of filling of the deep veins will be observed in the film. In this situation the superficial veins will be more completely outlined. The veins in the groin and pelvis can be visualized by injection of the internal saphenous vein in the thigh with a 50 or 75 per cent solution of diodrast.

The circumstances in which the venogram serves a useful purpose are classified under five headings: (1) In thrombophlebitis of the lower leg, to observe the proximal limit of the propagating clot, (2) when, in the absence of local signs, a patient complains of pain in the legs before or after becoming ambulatory following operation or prolonged illness, to confirm or dispel the suspicion of phlebitis which should always arise, (3) in iliofemoral thrombophlebitis, to determine the proximal extension of the clot or thrombus, (4) in chronic ulcer of the lower leg, when the phlebitic origin of the ulcer is not assured, and (5) in varicose ulcer, to determine the location and number of incompetent perforators at its base and in superficial thrombophlebitis, to determine the presence of concurrent deep phlebitis. These conditions will be discussed in the order named.

A—THROMBOPHLEBITIS OF THE DEEP VEINS OF THE LOWER LEG

In a previous report¹ routine division of the femoral vein was recommended in *all* patients known to have or suspected of having thrombophlebitis of the deep veins of the lower leg. This conclusion was derived from the fact (1) that there was no reliable guidepost by which to predict whether or not an embolus would occur, (2) that the incidence, morbidity and mortality from emboli were far greater than is generally realized^{7, 8, 14, 15, 16}. Since a dependable venographic technic has become available, we no longer divide the femoral vein on the basis of suspicion, but *always* if the signs and

symptoms are obvious or if a filling defect is demonstrable in the venogram

Examples of routine procedure are illustrated in the following six cases

Case 1—A female, age 32, one week after the birth of her second child, developed fever and pain in the right calf. The following day, examination showed tenderness in the right calf and fever persisted. There was no cyanosis, edema, ischemia or temperature change as compared with the opposite side. Venography showed a filling defect in one of the deep veins in the calf (Fig 1). Immediate division of the common femoral vein was performed. Fever disappeared promptly thereafter, pain subsided on the 3rd postoperative day, and she was allowed out of bed. She remained symptom free. Four weeks later she showed only the faintest degree of ankle edema, which disappeared completely after eight weeks.

Comment Although the venogram in this instance showed only a minor filling defect, the pain and tenderness were so outspoken as to leave no doubt of the diagnosis. We, therefore, regarded the risk of femoral vein division outweighed by the risk of embolus. The additional advantage of a short convalescence was a secondary consideration. According to Ochsner and DeBakey,¹⁷ a shortened convalescence is also achieved by paravertebral novocain block, but this technic does not, we feel, provide protection against the discharge of an embolus.

Case 2—A male, age 29, complained of pain in the right calf on the tenth day after repair of an umbilical hernia elsewhere. The pain increased in intensity, and on the 14th day it had spread to the groin. The entire leg was swollen. On the 15th day he developed cough, fever and pain in the left anterior chest. Intravenous heparin was given for four hours, twice daily, for seven days. The pulmonary signs cleared after five days of heparin therapy, but the leg remained painful for another 17 days. Swelling gradually subsided but recurred on the 36th postoperative day, when the patient got out of bed. He returned to bed at home for three weeks.

Two days after getting up, pain and swelling appeared in the *left* calf. He entered the Beth Israel Hospital three days later. On entry he had mild fever. Both lower legs were edematous, the left more than the right. The calf of the left leg was extremely tense and exquisitely tender on pressure, and Homans' sign was positive. There was no involvement of the veins of the thigh on the left side. Bilateral venography showed complete absence of filling of the deep veins of the lower legs. On the left side, the femoral vein was patent (Fig 2). Accordingly, a diagnosis was made of subsiding thrombophlebitis of the deep veins of the entire right leg and acute thrombophlebitis of the deep veins of the left lower leg. The left common femoral vein, which was found to be free of clot or inflammation, was divided. Pain rapidly subsided, the tension in the calf decreased and the patient was able to walk on the 4th postoperative day. Within a week he was fully ambulatory, and swelling of the left leg decreased rapidly. Seven months later the left leg was normal. The right leg was still edematous, the right ankle showed degenerative changes in the skin, and an area of increased warmth was present in the lower third of this leg.

Comment This patient had iliofemoral (and lower leg) thrombophlebitis on the right side. The impression that this condition does not involve a serious risk of embolism is not borne out in this and in other instances to which we shall refer later. The edema on the unoperated right side persisted

long after that on the operated left side presumably because of the more widespread involvement of the veins on the right side. Heparin did not prevent the onset of thrombosis on the left side.

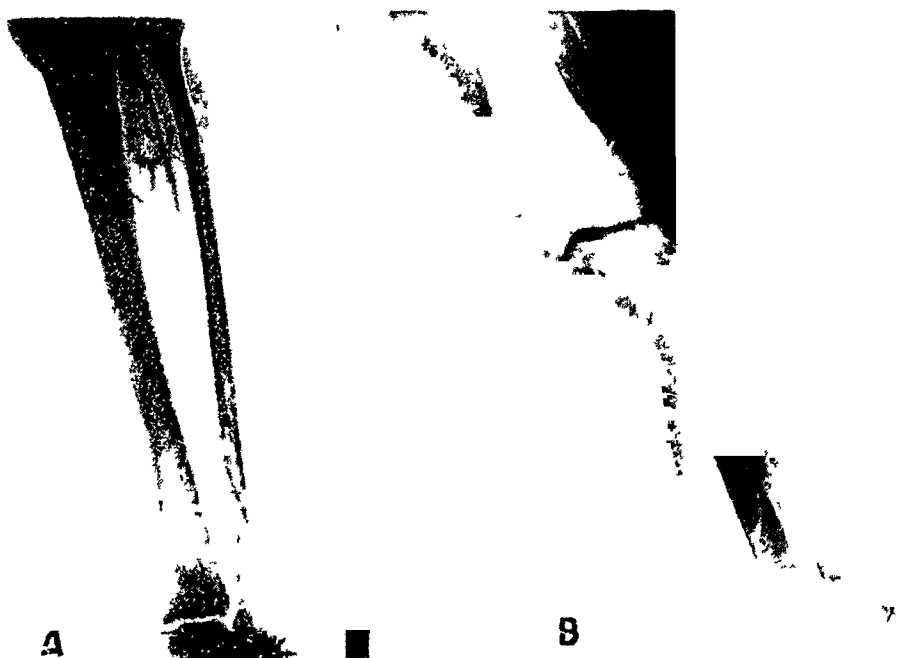


FIG. 2—Case 2. A. Right venogram showing complete absence of filling of the deep veins of the lower leg. B. Left venogram. The deep veins of the lower leg are not filled, but the femoral vein is patent.

Case 3—A male, age 36, complained of pain in the right shoulder and chest the day after removal of a plaster encasement, which had been applied to the left leg two weeks earlier for a fractured fifth metatarsal. He entered the hospital a week later, with a diagnosis of subsiding pulmonary infarct at the right base, and thrombophlebitis of the deep veins in the left lower leg. Examination revealed fever, a resolving consolidation in the right lower lobe and tenderness on pressure over the calf of the left leg which was very slightly swollen. Homans sign was positive. Bilateral venography revealed normal veins on the right, but complete absence of filling of the deep veins on the left. The left femoral vein, exposed under local anesthesia, like the artery, developed a marked spasm. No clot or thrombus was present. The vein was divided between ligatures caudal to the entrance of the profunda. Tenderness rapidly disappeared. Chest pain subsided by the 4th postoperative day, when he was allowed out of bed. Slight edema of the lower half of left leg was present. He was discharged from the hospital on the 7th postoperative day, capable of normal activity. Four months later the leg looked entirely normal.

Comment The undue persistence of pain and edema after sprains and fractures of the lower extremity will not infrequently be shown by venography to be due to phlebitis of the deep veins. The relatively high incidence of pulmonary embolism in major fractures of the lower extremities makes it worth while to have particular regard for signs of phlebitis in all such individuals.

Case 4—A female, age 44, diabetic, complained of tenderness in the right calf three days after a panhysterectomy and bilateral salpingo-oophorectomy. Homans' sign was positive. A right venogram was interpreted as showing early thrombosis without complete occlusion of the lumen. The right femoral vein was immediately divided below the entrance of the saphenous vein. No inflammatory process was present in or

FIG 3



FIG 4

FIG 3—Case 4. A. Right venogram. Incomplete filling of deep veins of leg. B. Left venogram. Absence of filling of deep veins of lower leg. Femoral vein fills normally.

FIG 4—Case 5. Normal filling of the iliac veins nine days after division of both common femoral veins.

near these structures and the lumen of the vein did not contain a clot. Edema of the ankle appeared and persisted, and some pain continued in the right leg. She was discharged ten days after division of the vein. Five months later she had edema only if she walked without an elastic support. She had slight pain and tenderness, just below the inner aspect of the knee, which was probably due to foot strain.

Case 5—A male, age 75, with generalized arteriosclerosis, hypertension and pulmonary emphysema, was out of bed on the 7th day after the second stage of a supra-

pubic prostatectomy. He started to walk on the 12th postoperative day. That evening the white blood count rose to 14,000. The next afternoon he became dyspneic, felt pain in the chest and showed congestion and multiple areas of increased density in the lower lung fields. Infarction was suspected. There was edema of both legs, more on the right, and moderate tenderness of the right calf. Bilateral venograms showed incomplete filling of the deep veins of both lower legs (Fig 3). Bilateral common femoral vein division was done the same evening. No clot was found at the level of division. The next morning he felt better, and became afebrile. The dyspnea, chest pain and tenderness in the right calf disappeared. He was out of bed on the second day after vein division. At the time of discharge the edema was much less than at the time of vein division. Bilateral pelvic venograms were taken through the saphenous vein, nine days after division of the common femoral veins. These showed normal filling above the site of division (Fig 4).

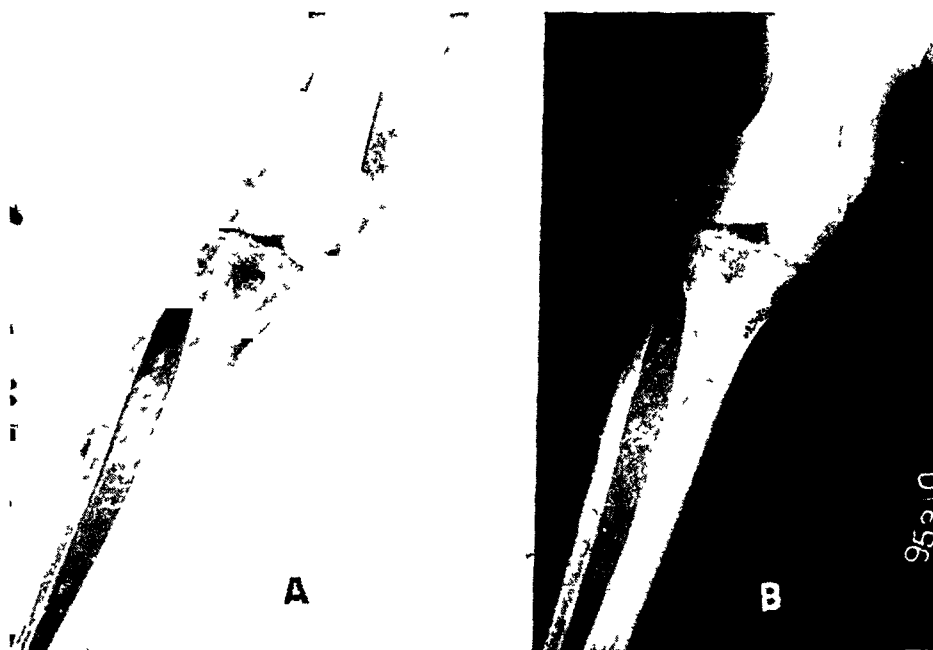


FIG 5—Case 6. Bilateral incomplete filling of deep veins of the lower leg. Both femoral veins are well outlined.

Case 6—A male, age 58, was ambulatory on the 17th day after a perineal prostatectomy. On the 19th day he complained of bilateral calf pain. Homans' sign was positive in the left leg, the calf of which was tender on pressure. No other signs of thrombophlebitis were observed. Venography was recommended but was not done until two days later, when, shortly after getting out of bed, the calf pain increased on both sides. The venograms showed bilateral lower leg thrombophlebitis (Fig 5). The following day the patient developed fever and pleuritic pain in the lower right chest, which showed râles and bronchial breathing. A roentgenogram showed infarction of the right lower lobe. That evening both common femoral veins were exposed under local anesthesia. They were free of clot or inflammation, and were divided between ligatures. Five days later the fever disappeared, and seven days later, when he was allowed out of bed, a roentgenogram of the chest showed almost complete clearing of the lung. Edema of both legs increased and reached a maximum after six months, at which time the patient reported that he had no complaints except a slightly heavy feeling in both legs.

Comment The increase in the edema after division of the femoral vein was probably due to postoperative increase in the extent of the thrombosis. That it may have been due to failure to interrupt the vasospastic reflex arc is possible.

The existence of a vasospastic reflex arc, which is broken by the operative procedure, is strongly suggested by the lessening or complete disappearance of edema in most instances of thrombophlebitis in the deep veins shortly after division of the femoral vein. The promptness with which it occurs has led us, as well as Honians,⁹ and Welch and Faxon,¹⁰ to perform ligation of the saphenous vein in the fossa ovalis for painful phlebitis of the superficial system, with gratifying results in nearly every instance. In two patients who had extensive thrombophlebitis of the saphenous vein, with pain and swelling unabated for four and eight weeks of bed rest, respectively, division of the vein in the groin resulted in prompt relief of symptoms and restoration to full activity within three days. Two other patients after a week of continuous pain below and above the knee from an acute phlebitis of the internal saphenous were up and walking in entire comfort on the day after division of the vein in the groin.

Formerly, we regarded division of the femoral vein below preferable to division above the vena profunda, because the latter was regarded as a large, useful collateral for venous return. We now consider the common femoral the more desirable site for the following reasons: (1) A substantial number

of thromboses occur in the profunda system, (2) the evidence for thrombosis in this system is not readily detectable clinically, or even with the aid of venography, except when the thrombosis is found at operation to have reached the mouth of the vein, and (3) significant postoperative edema cannot be shown to result from division of the femoral vein at any level, while division at the higher level is technically easier to perform.

The danger of overlooking the vena profunda is illustrated in the following cases:

Case 7—A male, age 53, was subjected to laminectomy for removal of an epidural fat pad compressing the spinal cord. Among other symptoms he had anesthesia to pain in the inner aspect of the thighs and lower abdomen. On the 4th postoperative day the temperature rose to 102° F. Examination of the lower legs for phlebitis was completely negative. Twenty hours later he suddenly became cyanotic and dyspneic, and death followed shortly thereafter. Postmortem examination revealed a massive

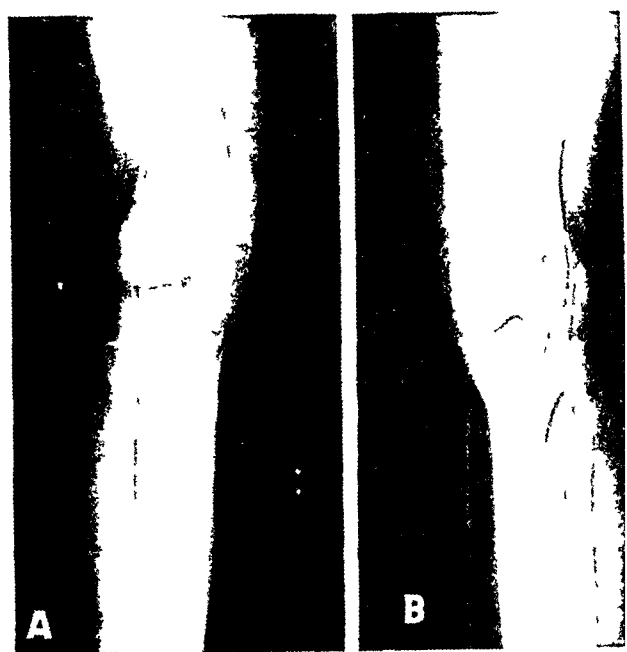


FIG. 6—Case 8. A. Right venogram. There is questionable normal filling of the deep veins of the lower leg. B. Left venogram. The deep veins of the lower leg do not fill.

pulmonary embolus arising from the right vena profunda, which contained a thrombus extending proximally into the iliac veins. The deep system below the vena profunda was not involved.

FIG 7

E



FIG 8

FIG 7—Case 8. A. Deficient filling of one branch of the deep veins in the right lower leg. B. Normal venogram of the left iliac veins.

FIG 8—Case 8. A. The right iliac and femoral veins above the site of division of the latter are well filled. B. The arrow points to a filling defect in the left femoral vein above the site of division.

Case 8—A male, age 60, had an uneventful convalescence following repair of a recurrent inguinal hernia until the 11th day, when he complained of pain and tenderness in the left calf. There was no swelling, fever or leukocytosis. He was allowed up in a chair two days later, although still complaining of left calf pain and tenderness. A positive Homans' sign was elicited. Venography showed a filling defect of the deep

veins below the femoral on the left side, a questionably normal pattern on the right side (Fig 6). That night the patient experienced right chest pain and showed physical signs and roentgenographic evidence of pulmonary infarction. The next morning, the 14th postoperative day, the venogram of the left leg was repeated. The previous filling defect in the left leg was again disclosed, and the left femoral vein *below the profunda* was divided. No thrombus or clot was seen. Occasional hemoptysis and signs of pleural effusion developed during the following week and mild fever persisted, but he was allowed in a chair on the 9th day after vein division. On the 11th day he suffered an attack of severe chest pain and cyanosis. A venogram of the left common femoral and iliac vessels showed no filling defect, but partial thrombosis of one venous trunk in the right lower leg was found (Fig 7), although there was no clinical evidence of phlebitis in this leg and the femoral vein filled well. The right femoral vein *below the profunda* was divided. No thrombus or clot was found at this level. The patient, however, continued ill with fever for 21 days, when he developed more fever, chest pain, dyspnea and signs consistent with a new pulmonary infarct. A normal ilio-femoral vein, above the level of division on the right, was demonstrated by venography, but a filling defect in the left common femoral above the site of division was found (Fig 8). Gradually recovery ensued. Painless swelling of the entire left leg appeared, but was not relieved by paravertebral novocain block. Seven months later he was back at work without disability, except for slight swelling of the left foot.

Comment This is an instance of failure to prevent embolism after bilateral division of the femoral vein below the profunda. Extension of a clot from the latter vein into the iliofemoral vein may explain the failure to prevent embolism. In another case, not described here, we had a similar experience. It was subsequent to these cases that we abandoned division below in favor of division above the profunda. Nevertheless, in the following case embolism occurred following bilateral division of the common femoral vein.

Case 9—A male, age 81, with coronary sclerosis, emphysema, severe secondary anemia, hypertension, an inguinal hernia, and a sigmoid carcinoma for 18 months, was submitted to cecostomy for acute obstruction of the colon. Immediate postoperative convalescence was satisfactory, but an unexplained vague discomfort in the chest and restlessness persisted. He was out of bed on the 7th postoperative day, but the chest discomfort and general debility did not improve. A week later there was clear evidence, confirmed by venograms, of bilateral lower leg thrombophlebitis. Bilateral division of the common femoral vein was done. These veins were free of clot or inflammation. Death followed 20 hours later. Autopsy revealed fresh antemortem clot above the site of vein division on the right side, and fresh antemortem clot below the site of vein division on both sides. In the deep veins of both lower legs a relatively old fibrosing thrombotic process was found. The lungs showed multiple old pulmonary emboli and a fresh antemortem clot straddling the primary division of each main pulmonary artery.

Comment The presumption is that this patient succumbed to a final embolus from a fresh clot which had formed in the right iliac vein subsequent to division of the right common femoral.

Case 10—(Quoted by permission of Dr. Louis Hermanson) A male, age 34, weighing 264 pounds, developed a bilateral lower lobe pulmonary complication the day after cholecystectomy for cholelithiasis. On the 4th day he felt vaguely uneasy in the chest and had right calf pain. A right venogram showed a filling defect of the deep veins up to the knee. The right femoral vein, which was free of clot or thrombus, was

divided below the profunda. Fever persisted, but he was allowed up on the 12th day. On the 15th day he went into collapse and showed the signs and symptoms of massive pulmonary embolus. A left venogram showed a filling defect of the deep veins up to the knee (Fig 9). The left femoral vein, which was free of clot or thrombus, was divided above the profunda. Mild edema of both legs was now evident. Slight fever persisted, but he was allowed up again on the 26th day, when he had another massive pulmonary embolus, with collapse, cyanosis and fall in blood pressure. Heparin was started immediately. Venography showed a filling defect in the right iliac vein, and a normal left iliac vein. Ligation of the right iliac vein was recommended but refused. Heparin was continued for 19 days, until the 45th day, when it was discontinued, and he was again allowed out of bed. A third massive pulmonary embolus occurred two days later (47th day). At the same time, vasospastic arterial occlusion occurred in the right upper and lower extremities. Return of blood flow was satisfactory in the right upper extremity a week later, and the cold blue right leg improved after three paravertebral novocain injections.

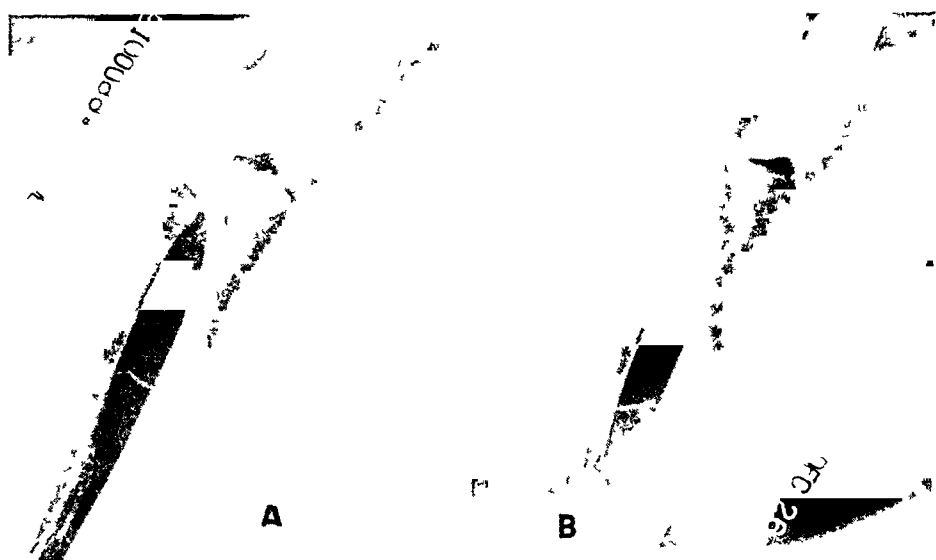


FIG 9—Case 10. A. The filling defect in the deep veins of the right leg involves the lower end of the femoral vein (at the arrow). B. The deep veins of the left leg do not fill.

After each attack of embolism fever rose to 104° F. Between attacks it varied from normal to 101° F. On the 63rd postoperative day, when fever increased, and râles in the right base and right pleural pain developed, venography of the iliac vessels was repeated. The left iliac vein showed a number of small filling defects, the right was not visualized owing to thrombosis of the right saphenous vein. The iliac veins were exposed transperitoneally. The left contained thrombus up to the entrance of the hypogastric vein, the right was surrounded by intense inflammatory reaction and was occluded by firm thrombus up to its junction with the vena cava. Both common iliac veins were ligated just below the inferior vena cava. He improved promptly, and continued to make a satisfactory convalescence.

Comment. It is evident from this and the previous case that femoral vein division cannot prevent thrombosis proximal to the site of division. This constitutes the chief limitation of this procedure for effective prophylaxis against embolism. But since it is an uncommon occurrence we feel justified in adhering to our position that routine division of the common femoral vein

is the procedure of choice in lower leg thrombophlebitis, unless, and until two conditions can be satisfied (1) That there is evidence that the act of division of the vein is *per se*, responsible for the development of thrombosis proximal to the site of division, and (2) that paravertebral novocain block or heparinization, *after thrombosis has occurred*, can be shown to prevent embolism as often as vein division

We must emphasize that we do not deny the great therapeutic importance of both heparin and novocain block. In appropriate circumstances each has indispensable value. For the prevention of embolism from lower leg thrombophlebitis, however, neither method should take precedence over division of the common femoral vein.

We are aware of the fact that the majority of such patients will eventually recover without surgical interference. Apart from the rapid rehabilitation which vein division achieves in most instances, deliberate failure to do so in any given instance is equivalent to deliberate acceptance of the risk of embolism in preference to the risk of division of the common femoral vein.*

The frequency with which wholly unsuspected pulmonary infarction or embolus has been found as the primary cause of death is evident from a number of sources. In three different series of routine autopsies, studied by McCartney,¹⁸ Collins¹⁹ and Hunter, *et al*,⁷ pulmonary embolism was the primary cause of death in 2-3 per cent. In 3,500 routine autopsies, Hampton and Castleman¹⁴ found pulmonary embolism the cause of death in 3-5 per cent, and pulmonary infarcts were present in 9 per cent. Belt⁸ found pulmonary embolus the cause of death in 6 per cent of 567 routine autopsies. Ten per cent of these cases showed pulmonary infarcts. The two latter reports point out that the number of infarcts found depends on the care with which the search is made. Hampton and Castleman¹⁴ found infarcts in 14 per cent of a carefully studied group of 370 autopsies. The discrepancy between the clinical and autopsy incidence of infarction is due to the widely divergent clinical pictures which infarction can produce. In our own experience, the roentgenologist, too, is frequently unable to distinguish between infarction and other pulmonary pathology.

The consequences of a hands-off policy in cases of lower leg thrombophlebitis have been described at some length by Fine and Sears,¹ but are worth illustrating by an additional experience.

Case 11—(Quoted by permission of another hospital) A female, age 60, with a negative past history, except for slight dyspnea on exertion and a ligation of a varicose left saphenous vein a year previous, entered the hospital complaining of dyspnea, pain in the right chest and shoulder and pain in the left calf. She had been in bed at home for eight days before admission because of pain in the left calf, especially on walking. The lungs showed râles and bronchial breathing at the right base, and a

* Regardless of the condition of the patient the morbidity and mortality of this operation in our hands has been *nil*, unless the development of thrombosis proximal to the site of division is regarded as a complication of the operation.

roentgenogram showed an infarct, presumably from phlebitis of the left lower leg. The process in the lungs cleared up completely shortly after admission. She became afebrile and apparently well. Toward the end of her stay the pain in the calf disappeared. A venogram showed a filling defect in the popliteal vein. Division of the femoral vein was considered, but an understandable difference of opinion as to the propriety of a relatively untried procedure led to a conservative management of the case. On the 15th day of her stay she was digitalized. She was allowed out of bed on the 17th day, when she suddenly went into collapse with cyanosis, fall in blood pressure and died in 30 minutes. Autopsy revealed a massive pulmonary embolus plugging the pulmonary conus. The heart was normal. No thrombus was found anywhere until dissection well down into the left thigh revealed a thrombus in the lower end of the femoral vein. The right leg veins were not involved.

There is a widespread mistaken impression that pulmonary embolism is usually a postoperative complication which is of no special concern to



FIG. 10.—Case 12. A The deep veins of the right leg filled normally. B The deep veins of the left leg are narrow and one main trunk is apparently in spasm. The bones obscure one well filled trunk seen in the original film.

the practitioner or the internist. It is evident that thrombophlebitis of the deep veins of the lower leg is a common disease in nonsurgical patients, and occurs, not infrequently, in active, apparently healthy individuals. In Hampton and Castleman's series of 370 cases of pulmonary embolism and infarction only 40 per cent were postoperative, 30 per cent were of cardiac origin, and 30 per cent were neither. In Belt's series of 56 cases of embolism only 16 followed surgery, and 40 occurred in nonsurgical conditions. Similar evidence is available from other sources 5, 6, 7, 15, 20, 21.

B—PAIN IN THE CALF ON FIRST BECOMING AMBULATORY AFTER OPERATION OR PROLONGED ILLNESS

This is a common complaint which is frequently ignored, especially when there are no concurrent objective signs to explain the cause of the pain. Occasionally such individuals succumb to a massive pulmonary embolus be-

fore or after leaving the hospital. The possibility of thrombophlebitis in the deep veins of the lower extremity should always be suspected and the diagnosis proved or excluded by doing a bilateral venogram.

Case 12—A female, age 50, developed atelectasis in the right lower lobe two days after resection of the sigmoid for carcinoma. The process in the chest cleared by the 11th day. Abdominal wound sepsis also developed, but steadily improved, so that she was allowed up on the 18th postoperative day. Two days later she complained of pain in the left calf. Calf tenderness was minimal, there was no increased heat, edema or cyanosis, and Homans' sign was negative. Bilateral venograms showed no filling defect, but one main deep trunk on the left was much narrower than normal (Fig. 10). This might have been due to venospasm, which at this stage of our knowledge would not warrant division of the femoral vein. The subsequent course was uneventful.

Comment In some six patients with a similar complaint the completely normal pattern of the veins allowed us to dismiss the suspicion of phlebitis and to discharge the patients. None developed phlebitis subsequently.

The decision for or against division of the femoral vein is occasionally difficult because minor filling defects in the venogram may be difficult to evaluate.

Case 13—A female, age 65, developed fever and pain in the left upper quadrant and in both calves on the 5th day after a subtotal gastrectomy and splenectomy for a large gastric ulcer. Bilateral calf tenderness with no other accompanying signs of phlebitis was found. Venography disclosed a small filling defect in the lower end of one of the deep veins of the left leg. The hesitation to proceed in this instance was followed by disappearance of fever and calf pain within 24 hours.

Comment When the signs and venographic evidence are minimal a decision to intervene may be difficult. Repeat venography, from day to day, can be done if necessary to fortify one's clinical judgment.

Occasionally a patient in bed with a protracted illness will complain of pain in one or both legs, which on examination seem to be entirely normal. A sensory neuritis due to a nutritional deficiency is commonly assumed, but thrombophlebitis may be present. Bilateral venography will establish or exclude this condition.

Case 14—A male, age 27, returned to the hospital two months after resection of the ileum and cecum for regional ileitis. Extension of the disease to involve all of the colon as far as the sigmoid was found, and ileosigmoidostomy was performed. The postoperative course was marked by fever and diarrhea. Five days after operation he began having severe bilateral calf pain. Examination of the legs revealed nothing abnormal. The fear that he might develop a pulmonary embolus from a possible thrombophlebitis was allayed by obtaining the venogram shown in Figure 11.

C—ILIOFEMORAL THROMBOPHLEBITIS

In the foregoing discussion we were primarily concerned with the therapeutic problem in phlebitis confined to the veins distal to the common femoral and usually arising in the deep veins below the knee. So-called "primary iliofemoral thrombophlebitis" is generally regarded as less likely to result

in pulmonary embolism⁹ This, if true, is adequate justification to avoid surgical interference The relative inaccessibility of the iliac veins is a sufficiently cogent deterrent as well In addition to several cases already presented, our experience in a recent study of a small group of patients with iliofemoral thrombophlebitis leads us to question the notion that embolism is a rare complication of this condition

Numerous attempts, including our own, to prevent embolism by the extraction of clots from these veins have been made with varying success^{9, 22, 23} This is to be expected—for removal of the clot may be incomplete, or, if the vein contains a thrombus, reformation and further extension may very well occur following extraction Although iliofemoral and lower leg thrombophlebitis are identical in the pathologic sense,* the former constitutes a different therapeutic problem chiefly because of the anatomic approach and the surgical hazard involved in attempting to shut off the site of origin of the embolus

When a diagnosis of thrombophlebitis of the lower extremity is made, the presence of tenderness in the groin or of edema of the thigh generally signifies the presence of clot or thrombus at least as far cephalad as the common femoral vein Ilio-femoral thrombophlebitis may, however, be present in the absence of edema of the thigh and in the absence of groin pain Since the extent of involvement of the common femoral and iliac veins cannot be predicted with certainty, venography through the internal saphenous in the thigh to demonstrate the degree of patency is worthwhile The prospect of a successful block above the site of the clot can thus be estimated If the external iliac is involved, division or ligation above the clot or thrombus is possible To accomplish this however is to undertake a procedure of major proportions It may, therefore, not be advisable to attempt prophylaxis against embolism *routinely* by ligation or division in these individuals Extraction of a loose clot *via* an opening in the common femoral vein is less hazardous, but less likely to be successful However, since the threat of death from embolism exists interference would seem to be justified It was for this reason that we felt it worth while to explore the veins in the group of cases which follow

Case 15—A male, age 70, five days after suprapubic cystotomy for prostatic disease, developed congestive failure which improved with digitalis and quinidine A roentgenogram on the 6th day showed an infarct in the right lower lobe It was not accompanied by symptoms On the 8th postoperative day the patient felt severe pain in the right calf, which was tender on pressure and showed thrombophlebitis in the short saphenous The long saphenous was dilated and prominent Venography showed complete absence of filling of the deep system of the entire leg, demonstrating the probable presence of iliofemoral thrombophlebitis (Fig 12A) From the right common

* The distinction between thrombophlebitis and phlebothrombosis made by Ochsner and DeBakey¹⁷ is, in our view, one of degree rather than kind So far as embolic complications are concerned, we can find no reliable distinguishing features which would allow us to judge when and when not to administer prophylactic measures

femoral vein, exposed in the groin, a thrombus, 22 cm in length, which included a valve from the mouth of the profunda, was extracted. The caudal half was red clot, the cephalic half was a firm white-gray thrombus. The common femoral vein was divided. Postoperatively, the right leg began to shrink, but the left leg began to swell. The next day calf pain and tenderness and a positive Homans' sign appeared in the left leg. The entire left leg was swollen and the left saphenous vein was distended. Ven-



FIG 11—Case 14. Normal right and left venograms.

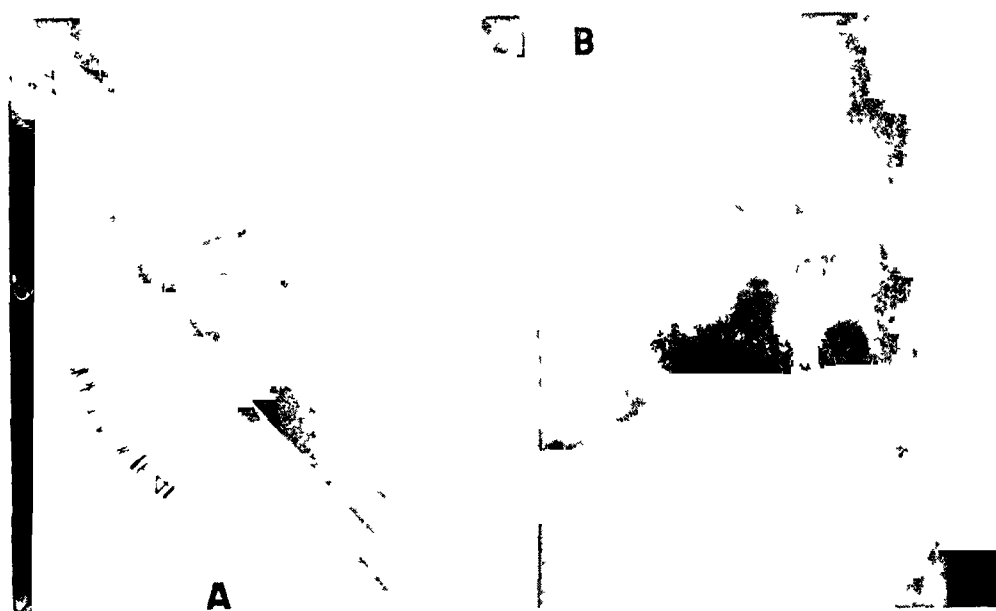


FIG 12—Case 15. A The deep veins of the left leg do not fill. B The left femoral and external iliac veins are dilated and partially filled with clot. Collateral venous channels are filled.

ography of the left common femoral and external iliac veins was done. This showed marked distention of the left common femoral vein, which seemed partially filled with clot extending into the external iliac (Fig 12B). Collateral venous pathways were also visualized. Exposure of the left common femoral showed marked perivenous inflammation. Large clots and thrombi were removed from the left external iliac vein. The common femoral vein above the saphenous was ligated. Swelling of the left leg rapidly subsided. Two weeks later he was discharged free of edema in both legs, and when seen six weeks later the legs were normal. Venography showed a filling

defect in the right common femoral and external iliac veins, which was probably due to an organizing thrombus. On the left side venography was not done because the saphenous vein had been tied off and could not be used for injection.

Comment In this patient the phlebotic process spread so rapidly, to involve the entire deep system, that one could not be certain where the process first began. The thrombus in the right femoral vein and the fresh red clot distally suggest that this may be an example of so-called "primary iliofemoral thrombophlebitis." It is possible, however, that a marked thrombophilic tendency can initiate the process in a number of areas simultaneously, with superimposed fresh clot extending in both directions. The pathologic studies of Neumann,⁵ Rosssle,⁶ and Hunter, *et al*,⁷ weigh the evidence in favor of the view that iliofemoral thrombophlebitis is in most instances a proximal extension of lower leg thrombophlebitis. In every case of iliofemoral thrombophlebitis which we studied by venography the deep veins in the lower leg were involved.

Case 16—A male, age 20, complained of pain in the right calf 13 days after nephrolithotomy. He showed a positive Homans' sign. There was increased heat, fever and leukocytosis, but no edema. The calf was tender on pressure and there was tenderness in the groin also. A venogram showed defective filling of the deep veins in the lower leg. The femoral vein was not visualized. It was exposed under local anesthesia in the groin. No perivenous reaction was present, but the vein was filled with a loose fresh clot extending into the external iliac. The extracted clot was 10 cm long. A few additional small clots were obtained by suction. The vein was then divided. Slight edema persisted for a week and on discharge the circumference of the right calf measured 0.5 cm greater than the left.

Comment It is debatable whether the thrombus began in the lower leg veins or the iliofemoral veins. It is impossible to claim that clot extraction avoided embolism, but it is fair to assume that the usual long convalescence which iliofemoral thrombophlebitis requires (*circa* 38 days for all types of thrombophlebitis²⁴) was markedly shortened by this procedure.

Case 17—A female, age 66, when allowed out of bed two weeks after cholecystectomy, complained of pain in the right lower leg and thigh. The calf and inner aspect of the thigh were tender on pressure. The superficial veins were varicose. There was slight cyanosis of the skin and swelling of the leg and thigh. Venography showed good filling of the superficial varicose veins, but the entire deep system failed to fill (Fig 13). Exposure of the veins in the groin showed perivenous inflammation. The great saphenous, common femoral and external iliac, for an indeterminate distance proximally, were filled with fresh unattached clot. The common femoral and external iliac were evacuated until blood flowed from above. Troublesome hemorrhage from two tributaries entering the common femoral posteriorly was controlled by ligatures placed from within the lumen of the femoral vein, which was then obliterated by suture. Division was avoided for technical reasons.

On the day of operation the entire leg was swollen. Five days later calf tenderness disappeared and the superficial veins were no longer distended. Nine days later she was up and walking, and 12 days later, after gradual disappearance of all symptoms and signs except slight swelling of the lower leg on walking, she was discharged. Three

months later the right leg and ankle were still somewhat painful and mild edema of the ankle occurred on walking. There was slight right calf tenderness and the right leg was slightly warmer than the left.

Comment Considerable bleeding in this patient makes it clear that the procedure of phlebotomy for clot extraction at this level can be a difficult one in certain circumstances.

In this instance the physical signs demonstrated involvement of the femoral vein and venography was not necessary for diagnosis. Nevertheless, even in obvious cases of phlebitis, venography is worth while, for it may reveal an extent of involvement not suspected from signs and symptoms alone.

Since the recovery of the preceding three patients was much more rapid than is ordinarily the case when conservative therapy is adopted, we believe that the operative procedure was beneficial. But two other patients with thrombophlebitis involving the entire deep system including the external iliac, from whose common femoral veins long thrombi were extracted, were not symptomatically improved. In one, the thrombus with superimposed clot was removed six hours after the diagnosis was made. Pronounced edema persisted for two months. In the other, pain and swelling continued for weeks afterwards.

Although, in the foregoing five cases, clot or thrombus extraction followed by division of the common femoral vein was not followed by embolus, the symptomatic relief achieved was satisfactory in only three. The claims made for heparin and for paravertebral novocain block, so far as symptomatic relief is concerned, are at least as good. Protection against embolism, however, is the factor of primary importance. For this purpose a comparative evaluation of all three methods is necessary. Perhaps a combination of methods may prove to be the best therapy.

Though we are on uncertain ground in deciding whether surgical intervention is justified before infarction has occurred, we should not hesitate to operate after a first infarct. To wait for a second infarct before operating as Lawen,²² and de Takats and Jesser²⁵ suggest, is too arbitrary a rule to be reliable. We regard a first infarct, however slight, a sufficient indication. The type of surgical procedure which should be adopted is by no means established. Lawen, Kulenkampff,²² and de Takats and Jesser, limited their efforts to clot extraction without division of the vein. Our view is in agreement with that of Homans, that division or at least ligation should be done whether or not complete extraction of clot or thrombus is achieved. Should embolism occur after emptying and dividing the common femoral vein, we would not hesitate to ligate or divide the common iliac vein.

D—PHLEBITIC ULCER

Chronic lower leg ulcers may be assumed to be of phlebitic origin if a satisfactory history of deep phlebitis is obtainable. In some instances the history will be negative or equivocal. Accurate diagnosis and proper therapeutic

tic procedure will be facilitated if the exact status of the deep veins can be ascertained

Case 18—A male, age 58, entered the hospital for a chronic ulcer which had been present for eight years. It began some months after removal of an encasement applied for a fracture of the upper third of the tibia. On admission to the hospital examination showed massive edema from the knee to the ankle, cyanotic engorgement of the lower third of the leg and a weeping ulcer involving about a third of the anterior surface of the lower leg. No varicose veins were seen. The patient stated that these had been cured by ligation in the groin two years previously at another hospital. A venogram showed almost complete obliteration of the deep veins and absence of the greater saphenous system (Fig 14). A nonvaricose, dilated lesser saphenous vein communicating with a venous trunk on the lateral aspect of the thigh was the sole remaining pathway for venous drainage. A diagnosis of phlebitic ulcer was assured and therapy applied accordingly.



FIG 13—Case 17. The deep veins do not fill. The superficial veins are varicose.



FIG 14—Case 18. The deep veins are almost entirely obliterated and the internal saphenous vein is obliterated. A lateral superficial trunk is the only significant venous trunk in the lower leg.

Comment The obliteration of the internal saphenous system two years previously was ill-advised, for the venogram demonstrates that the ulcer was not a varicose ulcer and that the saphenous system was the only major channel remaining for venous drainage of the lower leg.

Venography provides a technic for correct orientation in stubborn or complicated cases of disease in the veins of the lower leg. The disastrous effects of therapeutic obliteration of dilated saphenous veins, which are mistakenly assumed to be varicose, but which in fact have developed to compensate for an obliterated deep system, will thus be avoided.

Whether the veins involved in deep phlebitis ever recanalize to a degree

sufficient to restore appreciable function, is an unsettled question for which venography will presumably provide an answer. In the case cited here recanalization has not and probably never will take place.

An extreme example of a presumably permanent obliteration of the deep system is the following:

Case 19 A female, age 48, obese, mother of seven children, entered the hospital because of epigastric, periumbilical and left-sided abdominal pain of six weeks duration. There were no associated gastro-intestinal signs or symptoms. She gave a history of three attacks of deep thrombophlebitis of the lower extremities, one of which, 13 years ago, after childbirth, was bilateral and very severe. Aside from obesity and hypertension, physical examination was negative except that the superficial veins of the lower left half of the abdominal wall were indurated, tender, and more prominent than usual. Superficial varices were observed in both lower extremities, those on the left were reddened and tender. The abdominal pain was attributed to phlebitis of the veins in the abdominal wall, probably including the veins in the falciform ligament. Venography of the lower extremity showed complete absence of the deep veins in the right leg and pelvis with gross dilatation of one collateral channel in the abdominal wall. On the left there was nearly complete obliteration of the deep system of the veins in the leg and pelvis, with numerous small collateral channels in the abdominal wall, some of which were presumably blocked by the active thrombophlebitis.

E—VARICOSE ULCER AND SAPHENOUS THROMBOPHLEBITIS

The venogram can be useful to locate the position and number of incompetent perforators in the bed of a varicose ulcer which persists following oblitative therapy of varicose saphenous veins.

We have already referred to the accelerated rate of recovery in superficial thrombophlebitis by division of the saphenous vein in the groin. The following is an instance of septic thrombophlebitis beginning in the saphenous system.

Case 20 A female, age 50, diabetic, was submitted to ligation of a varicose left internal saphenous vein in the groin. Wound sepsis followed and spread to the surrounding tissues, requiring multiple incisions. Repeated chills, fever and positive blood cultures established the diagnosis of *Staphylococcus albus* septicemia or pyemia, which did not subside in spite of adequate sulfathiazole and sulfadiazene therapy. Ligation of a vein containing the septic thrombus, which was considered responsible for the generalized infection, required a knowledge of the status of the deep veins. A venogram showed complete obliteration of the deep system in the lower leg. Since the infectious process began in the groin the deep veins at this level were presumably also involved. A venogram of the iliofemoral veins could not be taken because of the obliteration of the saphenous system. It was obvious that nothing could be accomplished by an approach below the inguinal ligament. The left iliac vein was exposed through an extraperitoneal incision, and the proximal end of the thrombus was located at the beginning of the common iliac, which was ligated. Eventual subsidence of the generalized and local infection took place.

Extension of thrombophlebitis from the saphenous to the deep system is not rare. If the process in the internal saphenous vein extends into the groin, a venogram will be useful as a guide to therapy. We, like Welch and Faxon¹⁰, have found deep phlebitis of the lower leg by venography when a superficial phlebitis in the external saphenous system obscured the local evidence in the calf muscles. Division of the deep as well as the superficial veins is advisable in this situation.

SUMMARY AND CONCLUSIONS

Further experience, based on a policy of division of the femoral vein for the prevention of embolism in *all* cases of thrombophlebitis of the deep veins in the lower leg, has led us to the following conclusions

1 Division of the common femoral vein will cause early resolution of the thrombophlebitic process in the lower leg. Edema of the lower leg appears not to be aggravated, indeed the process frequently disappears more rapidly than might be expected. In occasional instances edema increases after vein division, but we are not aware of a valid reason for attributing the result to vein division.

2 Our former practice of dividing the femoral vein, by preference below the entrance of the vena profunda, has been abandoned in favor of division above, because of an occasional instance of embolism from the vena profunda.

3 When thrombophlebitis of the lower leg is present, division of the common femoral vein is preferable to heparinization or paravertebral novocain block *as a prophylactic measure against embolism*. We do not wish to imply that vein division is superior to these measures for the treatment of the local process *per se*.

4 There are occasional individuals in whom the process does not remain confined to the deep veins in the lower leg. A new focus of thrombosis above the site of vein division may develop and embolism may then occur. In this event the patient must be reclassified as one with iliofemoral thrombophlebitis and treated accordingly.

5 The treatment of iliofemoral thrombophlebitis by clot or thrombus extraction *via* the common femoral or iliac veins, followed by division of either of these veins is a valuable and at times indispensable procedure, but we do not feel that it need be adopted as a routine measure. Heparinization or paravertebral novocain block may be as satisfactory or even superior for the purpose of securing symptomatic relief. However, if one infarct should occur, regardless of what type of management has been in effect, it is our view that division of either the common femoral or iliac vein above the site of, or after extraction of, the clot or thrombus should be performed.

6 Venography is an indispensable technic for the correct management of all types of thrombophlebitis of the lower extremity. A filling defect in the venogram does not prove the presence of thrombophlebitis unless the element of vasospasm can be ruled out. Until an effective method for achieving this during venography becomes available the venogram should be interpreted in the light of the concomitant clinical picture.

7 The varying circumstances in which venography can be useful are described.

BIBLIOGRAPHY

- ¹ Fine, J, and Sears, J. B. The Prophylaxis of Pulmonary Embolism by Division of Femoral Vein. *ANNALS OF SURGERY*, 114, 801, 1941.
- ² Barker, N. W., Nygaard, K. K., Walters, W., and Priestley, J. T. A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism. *Proc Staff Meet., Mayo Clinic*, 15, 769, 1940, 16, 1, 17, 34, 1941.

- 3 Pilcher, R Postoperative Thrombosis and Embolism *Lancet*, 2, 628, 1939
- 4 Frykholm, R Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis *Surg, Gynec, and Obst*, 71, 307, 1940
- 5 Neuman, R Centers of Origin and Forms of Development of Thrombosis of the Leg *Arch f path Anat*, 301, 708, 1938
- 6 Roessle, R On the Significance and Origin of Venous Thrombosis of the Lower Legs *Arch f path Anat*, 300, 180, 1937
- 7 Hunter, W C, Sneed, V D, Robertson, T O, and Snyder, G A C Thrombosis of the Deep Veins of the Leg *Arch Int Med*, 68, 1, 1941
- 8 Belt, T H Thrombosis and Pulmonary Embolism *Am J Path*, 10, 129, 1934
- 9 Homans, J Thrombosis of Deep Veins of Lower Leg Causing Pulmonary Embolism *N E Jour Med*, 211, 993, 34 Venous Thrombosis in Lower Limbs *Am Jour Surg*, 38, 316, 317 Circulatory Diseases of Extremities Macmillan, 1939 Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Leg *N E Jour Med*, 224, 179, 1941
- 10 Welch, Claude E, and Faxon, Henry H Thrombophlebitis and Pulmonary Embolism *J A M A*, 117, 1502, 1941
- 11 Sears, J B Experience with Femoral Vein Ligation for Prophylaxis of Postoperative Pulmonary Embolism *N E Jour Med*, 224, 108, 1941
- 12 Ochsner, A, and DeBakey, M Therapy of Phlebothrombosis and Thrombophlebitis *Arch Surg*, 40, 208, 1940
- 13 Bauer, G Venographic Studies of Thrombo-Emboic Disease *Acta Skand Chir*, Supplement 61, 1940
- 14 Hampton, A O, and Castleman, B Correlation of Postmortem Chest Teleroentgenograms with Autopsy Findings *Am Jour Roentgenol*, 43, 305, 1940
- 15 Johnson, A S Antemortem Recognition of Pulmonary Embolism *N E Jour Med*, 222, 793, 1940
- 16 Barnes, A R Pulmonary Embolism *J A M A*, 109, 1347, 1937
- 17 Ochsner, A, and DeBakey, M Therapeutic Considerations of Thrombophlebitis in Phlebothrombosis *N E Jour Med*, 225, 207, 1941
- 18 McCartney, J S Quoted by Barnes, A R¹⁶
- 19 Collins, D C Pulmonary Embolism Based upon a Study of 271 Instances *Am J Surg*, 33, 210, 1936
- 20 Barker, N W Primary Idiopathic Thrombophlebitis *Arch Int Med*, 58, 147, 1936
- 21 Culp, O S Postoperative Venous Thrombosis and Pulmonary Embolism Analysis of 88 Cases *Bull Johns Hopkins Hosp*, 67, 1, 1940
- 22 Lawen, A Further Experiences with Thrombectomy in Venous Thrombosis *Arch Klin Chir*, 193, 723, 1938
- 23 Kulenkampff, D The Prevention of Severe and Fatal Emboli by Evacuation of the Iliac Vein *Arch Klin Chir*, 193, 727, 1938
- 24 Linde, S On the Incidence of Thrombo Embolism Following Surgical Operation, and its Influence on the Length of the Recumbent Period *Acta Medica Scand*, 107, 165, 1941
- 25 de Takats, G, and Jesser, J H Pulmonary Embolism *J A M A*, 114, 1415, 1940

DISCUSSION—DR HERMAN E PEARSE (Rochester, N Y) Dr Fine has given a very excellent discussion of the treatment of this condition, and I would like to add one word on its prevention Welch showed that one essential factor in the propagation of intravascular clotting was stasis The postoperative period is one of stasis in the veins of the lower extremities I believe that much of this intravascular clotting can be prevented by adequate leg exercises in the immediate postoperative period

DR ALTON OCHSNER (New Orleans La) I am sure we are all deeply indebted to Dr Fine for this presentation relative to thrombophlebitis In our experience, we believe one must differentiate between two types of clotting, namely those in which there is

inflammatory disease and those in which there is no inflammation which we have designated as phlebothrombosis. In both of these there are the same factors responsible, i. e. the changes in blood constituents which are the result of tissue damage. These may be the result of trauma, the result of invasion by infection, or neoplastic disease.

In the patient with thrombophlebitis we feel with few exceptions unless suppuration has occurred ligation of the vein is not necessary because in these instances the clot is firmly attached and there is no danger of it becoming detached. If one will treat these patients by wrapping the extremity and preventing propagation of the thrombus above the area of thrombophlebitis there is little danger of detachment of the clot. These we feel are best treated by novocain block of regional sympathetic ganglia. We have had prompt subsidence of symptoms.

There are a few cases of thrombophlebitis and this is particularly associated with pelvic thrombophlebitis in which ligation of the vein is necessary. These are infected emboli. Recently Dr. Conrad Collins, of the Department of Gynecology, has tied off eight vena caval successfully in patients who had puerperal infections with infected emboli breaking off.

In the patient who has a phlebothrombosis there is little evidence of disease. It is this patient who gets up out of bed after operative procedure and develops embolism. We can detect these by suspecting and I know no condition in which suspicion is more valuable. It has become a rule in our clinic that any patient past forty years of age, who has an operative procedure or who has an inflammatory process or neoplastic disease has careful routine examination of his lower extremities. We measure the extremities and not only perform the Homan's test which is the dorsal flexion of the foot but carefully examine the plantar aspects of their feet because this is one of the areas in which the thrombi may originate. In these individuals if there is some tenderness phlebography must be done and if the phlebogram shows a defect then the vein should be tied off. We not only tie off the vein but we suck out the clot proximal to the wound which I am sure Dr. Fine does too.

It is of importance I think to realize that heparin will not necessarily protect these cases. I have recently seen a patient who had five emboli four of which occurred in 21 days during which time he received heparin continuously. His clotting time ranged from 15 minutes to one-half hour. It was only after his fifth one that a phlebogram was made and his vein was tied off which prevented a fatal outcome.

If one will recall that 71 per cent of the patients who have fatal pulmonary emboli have had an antecedent infarction it certainly is an indication to us that any patient who has infarction should at least be given advantage of a phlebogram. By means of phlebography, with the exceptions which Dr. Fine has brought out namely spasm, and possibly some cases in which there is absence of filling one can determine quite accurately whether there is a clot or not and the ligation of the vein in such an instance is certainly life-saving.

DR. LELAND S. MCKITTRICK (Boston, Mass.) I would like to say just a word in support of what Dr. Fine has talked to you about. We in the Peripheral Vascular Clinic at the Massachusetts General Hospital have been much interested in this group of patients. We are not able—and I say this with apologies—to draw this clear-cut distinction that Dr. Ochsner has just spoken to you about between the two groups that he has so ably described. Heparin has let us down or possibly we have let heparin down. In any case we have not received from heparin the same satisfactory results that the group in Toronto has.

In our Peripheral Vascular Clinic we have a group which I think speaks quite independently. Sometimes we agree and frequently we disagree. The group is in complete agreement upon the value and importance of an attack upon the venous tree in cases of thrombophlebitis or phlebothrombosis (I am including them all together). We also are in complete agreement upon the safety of the method. We are in agreement upon the difficulty of interpreting the venograms particularly those of the veins below the level of the popliteal.

We are in complete disagreement as to the technic of obtaining venograms. We are in disagreement as to their importance because of the doubt in the minds of many of us at the present time as to whether we can interpret venograms with sufficient accuracy to give them more significance than a very careful clinical examination of the part. We are in disagreement as to the level at which the vein should be opened and ligated.

I say 'opened and ligated' because the vein should never be constricted until it is first

opened to exclude the presence of a thrombus at the level at which the ligature is to be applied

So I leave it at that point. We believe in the procedure, at least in the principles of it, but the many, many things about which we are not in agreement make this a particularly lively and interesting subject at the present time.

DR JACOB FINE (closing). With reference to Dr Ochsner's distinction between thrombophlebitis and phlebothrombosis, I think the detailed text of this paper will show that from the point of view of embolism this distinction is not helpful clinically, for we have seen embolism in individuals with outspoken thrombophlebitis.

Dr Pearse's reference to leg exercises to minimize the occurrence of venous thrombosis is well taken. We adopted that principle in our clinic years ago and I think it is a well known principle, but unfortunately we continue to get thrombosis in spite of the use of leg exercises.

As to ligation *versus* division of the vein, we are in complete agreement with what Dr McKittrick says. We always divide the vein, but we always open it before dividing it, and if there is a clot at the site of the femoral vein it is removed. If it cannot be removed, we consider it desirable to divide the iliac vein if embolism has occurred or if it occurs subsequently.

ANNOUNCEMENT OF FELLOWSHIPS IN MEDICINE AND PUBLIC HEALTH

THE COMMONWEALTH FUND of New York, a philanthropic foundation established in 1918 by the late Mrs Stephen V Haikness, announces that it is offering through the Pan American Sanitary Bureau fifteen fellowships for one year's study of public health subjects or postgraduate medical courses to properly qualified persons who are citizens of the other American republics. Fellowships in public health will be open to physicians, sanitary officers, technicians, public health nurses, etc. These fellows will be selected through a system of cooperation with medical and health authorities of the different countries concerned, and whenever deemed advisable they will be interviewed by traveling representatives of the Pan American Sanitary Bureau. Each fellowship will provide living allowances while the holder is in the United States, travel costs, and tuition. Knowledge of the English language will be among the requirements, and also the possession of certain specific qualifications.

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THE CONTROL OF HAIR AND FEATHER PIGMENTATION AS REVEALED BY GRAFTING MELANOPHORES IN THE EMBRYO

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THIS TALK DEALS with the mechanism of pigmentation in hairs and feathers, one of the major problems in animal biology. You are already familiar with variations in the color of human hair, also with the fact that many animals show regional differences in the color of the hair or feather—as, for example, the spotted patterns of the Dalmatian dog, the leopard, Holstein cow or the guinea fowl and with the striped patterns of the zebra, tiger and the Barred Plymouth Rock feathers. It is not my intention this morning to present an explanation of how these color patterns are produced but merely to give you a glimpse into the nature of the problem involved in their formation.

Specifically, we shall examine (1) the source of the pigment cells in the embryo, and (2) the mode of formation of pigment in hair and especially in feathers which have been studied much more extensively.

Method—The method which we use in our experimentation is to graft small bits of tissue (usually less than one millimeter in greatest dimension) from one embryo, the donor, into another embryo, the host. The host chick embryo is prepared for receiving the graft by first sawing a window by means of a hacksaw in the shell directly over the embryo, whose exact position is located by candling. The shell window is removed, and the shell membrane is slit open so as to expose the body of the embryo. The embryo is now viewed through a binocular dissecting microscope and a small incision is made in the body wall for receiving the graft tissue. Next, the piece of tissue which has been isolated from the donor embryo by means of fine steel dissecting needles is transferred to the host embryo and pushed into the graft incision. The shell window is then returned to its position and sealed in by means of melted paraffin, and the egg returned to the incubator.

The Source of Pigment Cells—From several lines of evidence (for a detailed consideration see Rawles 1940, Ris 1941, Willier 1941 and Willier and Rawles 1940) it has been proved that the precursor pigment cells arise in the neural crest and migrate into the skin and its derivatives, the hair and feather follicles. Two main types of experiments will be presented here. The wing-bud is excised from an embryo of a pigmented breed of fowl, the Barred Plymouth Rock, and grafted into the coelom of a White Leghorn host chick embryo. A wing-bud from an 85-hour embryo grown in the coelom of the host embryo develops into a normal-appearing wing covered

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with black down feathers, as you would expect since it came from a Barred Rock donor. If, however, the same experiment is done using a wing-bud from a donor embryo of 70-hours incubation the result is quite different. A normal wing forms but is covered with skin having white down feathers. These results show that the pigment cells arise outside of the wing-bud and migrate into it between 70 and 85 hours of incubation.

My research assistant, Dr. Mary E. Rawles (1940), has carried out similar experiments with the mouse embryo. A strain of genetically black mice was used. The mouse embryo at about 11 days of gestation is removed from the uterus and pieces of skin ectoderm are isolated from two regions of the embryo: one over the neural crest and one from the forelimb-bud. If the skin ectoderm contains neural crest cells it will produce, when transplanted to the coelom of a White Leghorn host embryo, typical skin and hair follicles, including pigment cells. If, on the other hand, a piece is taken from the limb-bud of the same embryo the result is the same except that there are no pigment cells whatsoever present in the hair follicles. By means of these two types of analysis along with certain other experimental evidence (Ris, 1941), we have been able to prove conclusively that the pigment cells are derived solely from the neural crest. Moreover, the results show that the neural crest cells migrate laterally and invade the skin, the hair and feather follicles and furnish melanin pigment to these structures. In the absence of neural crest cells the hair and feather develop normally but without any pigment.

Grafting of Precursor Pigment Cells—In this type of experiment neural crest cells (potential melanophores) are grafted from one embryo to another of equivalent ages, i.e., about 70-hours incubation. The donor and host embryos are of different breeds or species of bird. Neural crest cells from the donor are transplanted to the base of the wing-bud of the host before its own neural crest cells have migrated into the wing-bud. This results in the formation of an area of donor-colored down feathers on the wing and adjacent regions of the body in a majority of cases. The down plumage is replaced by juvenile contour feathers having the shape, rate of growth and distribution in tracts characteristic of host control chicks, but invariably having the color or color pattern of the donor breed or species. This was found to be true for all donor breeds and species tested such as Barred Plymouth Rock, New Hampshire Red, Black Minorca, Brown Leghorn, White Wyandotte, White Silkie and White Plymouth Rock, crow, robin, ring-neck pheasant. The results are interpreted to mean that grafted melanophores enter the wing before the host ones do and take up all the available positions in the skin and feather follicles. The host melanophores migrate later into the wing from their seat of origin in the neural crest. Since, however, they have entered later than the donor melanophores, they remain outside of the feather follicles in the dermis of the skin.

Cooperation of Donor Melanophores and Host Feather Follicle—It is thus clear that two component parts differing in their genetic constitution

cooperate in the production of the donor colored feathers in the host. The feather follicle is the embryonic organ which builds the structural elements of the feather. The melanophore furnished by the donor, on the other hand, is the pigment producer. The melanophore is a branched cell containing melanin pigment granules. When introduced into the host embryo the melano-



FIG. 1.—A 29 day old White Leghorn male chick showing barred plumage on the right wing and breast. Produced by grafting potential melanophores from an 18 hour old Barred Plymouth Rock embryo into the base of the wing bud of the host embryo at 79 hours incubation.

FIG. 2.—A 22 day old Barred Plymouth Rock chick showing white plumage on the right wing. Produced by grafting neural crest cells (potential melanophores) from a 71 hour old White Silkie Bantam embryo into the base of the wing bud of the host embryo at 70 hours incubation.

phores from pigmented breeds of fowl migrate into the developing feather follicle and take up positions next to the epidermal cells forming the parts of the feather. The melanophore sends out several processes which come in close approximation to the epidermal cells. The tips of the processes extrude pigment granules which are taken into the host epidermal cells. The granules which the host epidermal cells thus acquire are donor specific as to size, shape, and color. When melanophores from the white breeds of fowl are grafted to pigmented breeds, they migrate into the host feather follicles just as melanophores from pigmented breeds do, but die before depositing any pigment granules, hence a white host feather is produced. Apparently the melanophore of the white breeds possess a lethal factor which brings about its early death.

The question now arises as to how donor melanophore and host feather follicle work together in the production of a specific coloration or color pattern. That the donor melanophores react to extrinsic factors in the host feather follicles is illustrated by the striking variations in color pattern produced in the various feathers of the same bird. Barred Rock melanophores in a White Leghorn host produce color patterns, ranging from those almost wholly black to those with distinct black and white bars. Measurements of the increase in length of the growing feather show that if the growth rate is rapid (certain flight feathers) the feather tends to be all black except for traces of white bars on the shaft and when slow (breast feather) the black and white bars are distinct and nearly equal in width. Generally speaking, rapid growth rate favors a greater deposition of black pigment than a slow rate.

Similar variations in color pattern have been produced by guinea fowl melanophores in White Leghorn host feathers. In rapidly growing feathers the vane is gray with tan-brown tips and the outer vane margins are mottled brownish-gray. In slowly growing ones the feather shows cream-white bars on a gray background. Thus another example is furnished showing that the color pattern formed varies with the rate of growth and position of the feather on the host. It ranges from a mottled pattern to one which is typically barred.

Summarizing then, it is evident that the individual feather follicle alters greatly the type of pattern produced by the donor melanophores. Each feather follicle produces its own specific type of pattern.

Rôle of Hormones in Feather Pigmentation—That endocrine substances have an effect on melanophores is brought out in various ways. Lille and his associates (Lille, 1932) have shown that thyroxin injected into Brown Leghorn males affect profoundly the pigmentation pattern produced in a regenerating neck hackle feather. The thyroxin produced an extension of the black pigment. By controlling the dosage and time of introduction interesting atypical pigmentation patterns can be produced in the feather.

Also, these investigators have shown that sex hormones may also modify feather color patterns in the Brown Leghorn fowl. In this fowl the breast

feather is black in the normal male and capon and salmon-colored in the normal female. If a breast feather of a capon is plucked and the female sex hormone estrone is injected at suitable times during its regeneration, a salmon-colored bar is formed across the feather vane. Thus a female colored bar is produced on a male colored background. Similarly male colored bars may be produced in regenerating breast feathers by omitting every seventh day an otherwise daily injection of female sex hormone. In these experiments we have evidence that the female hormone favors the differentiation of a type of melanophore which deposits salmon-colored pigment.

Recently Hamilton (1941), working in my laboratory, has studied the action of the sex hormones and desoxycorticosterone on the differentiation of melanophores cultivated in plasma clots *in vitro*. He found that skin ectoderm explants of the N. H. Red embryo both estrone and testosterone propionate bring about the differentiation of red melanophores (typically only infrequently present in control cultures). Also the adrenal hormone desoxycorticosterone, has an inhibitory action on the differentiation of Barred Rock melanophores. If a piece of skin ectoderm from a seven-day embryo of this breed is cultivated in a plasma clot containing 100 *gamma* of this substance per cubic centimeter no melanophores differentiate. If the clot contains 67 *gamma* per cubic centimeter many degenerate melanophores are found along with a few expanded ones.

These experiments show that melanophores have the capacity to respond to hormones and thus furnish a basis for understanding the role of hormones in feather pigmentation.

SUMMARY

1 Melanophores arise from the neural crest and migrate into the skin and its derivatives, the hair and feather follicles.

2 Hair and feather follicles build the hair and feather, respectively. In the absence of melanophores both hair and feather are white but normal structurally.

3 Melanophores from pigmented breeds of fowl deposit specific melanin pigment granules into the epidermal cells of the host feather. Melanophores from white breeds penetrate the feather follicles of potentially pigmented hosts but deposit no pigment granules. These are lethal cells which die before they have time to deposit pigment granules. A genetic lethal factor in the melanophore is postulated as causing gray hair in man.

4 By grafting melanophores from one breed of chick embryo to another it is possible to show the respective roles of the melanophore and feather follicle in the formation of pigmentation patterns. The specific color or pattern produced depends upon the genetic constitution of the melanophore and partly upon the physiology of the feather follicle, i.e., its growth rate, reaction threshold, etc. They work together in forming a specific color pattern.

5 Hormones modify greatly the direction of differentiation and action

of melanophores They have a profound effect on the melanophores during the process of color pattern formation in a developing feather

REFERENCES

- Hamilton, H L Influence of Adrenal and Sex Hormones on the Differentiation of Melanophores in the Chick Jour Exp Zool, **88**, 275-305, 1941
- Lillie, F R The Physiology of Feather Pattern Wilson Bulletin, **44**, 193-211, 1932
- Rawles, Mary E The Development of Melanophores from Embryonic Mouse Tissues Grown in the Coelom of Chick Embryos Proc Nat Acad Sci, **26**, 673-680, 1940
- Ris, Hans An Experimental Study on the Origin of Melanophores in Birds Physiol Zool, **14**, 48-66, 1941
- Willier B H An Analysis of Feather Color Pattern Produced by Grafting Melanophores during Embryonic Development Amer Nat, **75**, 136-146, 1941
- Willier B H, and Rawles Mary E The Control of Feather Color Pattern by Melanophores Grafted from One Embryo to Another of a Different Breed of Fowl Physiol Zool, **13**, 177-199, 1940

AN EXPERIMENTAL APPROACH TO THE PROBLEM OF MENSTRUAL DISORDERS*

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FOR THE PAST 13 YEARS our little group has been engaged in an experimental study of the disorders of menstruation. Our purpose is to discuss, briefly, the experimental approach to this problem, to describe some of our current experiments, and to relate these to past work and to the problem as a whole.

Primarily, the phenomenon of menstruation is an expression of endocrine activity, by means of ovarian hormones, the endometrium is stimulated. Later, as a result of certain changes in the concentration of the hormones, the endometrium undergoes a phase of regression which is characterized by the appearance of menstruation. The problem of abnormal menstruation can, therefore, be said to have a central phase dealing with various lesions of the endocrine system, a hormonal phase which deals with the ebb and flow of the ovarian hormones and a peripheral phase dealing with the vascular changes in the end-organ or endometrium.

For descriptive purposes it is best to begin with the changes in hormone concentration which are responsible for the initiation of menstruation. Many observers had noted the premature appearance of menstruation following the removal of a corpus luteum or oophorectomy. Allen¹ observed a similar premature menstruation in monkeys subjected to castration and also noted the premature appearance of menstruation following surgery to large graafian follicles. In further experiments, Allen injected castrated monkeys with estrogen in oil for nine to 20 days. Three to ten days after the cessation of estrogen injections, menstruation appeared. Many investigators have confirmed this observation of uterine bleeding in castrated individuals following the cessation of treatment with estrogen. Such estrogen-withdrawal bleeding can be indefinitely postponed by following the estrogen treatment with progesterone, but when the progesterone is discontinued, bleeding occurs. Bleeding does not occur during treatment with ovarian hormones as long as the amount of hormone available remains above a certain so-called critical level. It may occur during treatment with estrogen if the daily dose is suddenly reduced below this level, or if estrogen withdrawal is followed by treatment with small daily doses of progesterone. If both hormones have been administered, bleeding occurs following progesterone withdrawal, even when estrogen

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gen is continued in amounts which would have been sufficient to prevent bleeding had no progesterone been given. If, in these circumstances, very large amounts of estrogen are given following progesterone withdrawal, bleeding may not occur until after the estrogen injections are discontinued.

These facts, and many others of similar import, have led to the conclusion that a decline in the level of ovarian activity is an essential prerequisite for the onset of menstruation.

The vascular phenomena characteristic of normal menstruation in the rhesus monkey have been described by Markee,² who observed the process in bits of endometrium transplanted to the anterior chamber of the eye. Decrease in the size of the intra-ocular transplants always precedes and accompanies menstrual bleeding. When the area of the transplant has decreased 20 to 30 per cent, the circulation in the superficial part of the endometrium becomes slower and slower until a condition of stasis or near stasis exists. Four to 24 hours before bleeding begins, the coiled arteries which supply the upper one-half to two-thirds of the endometrium constrict, rendering the whole transplant ischemic. Vasoconstriction persists throughout the menstrual period. However, following the initial period of ischemia, individual arteries relax temporarily, a few at a time, and when this happens, hemorrhage occurs. Most commonly, blood escapes through a break in the wall of an arteriole or capillary and forms a hematoma which subsequently ruptures. It may break through the uterine epithelium without forming a hematoma. Also, diapedesis with or without hematoma formation may occur and a venous flow may take place in fields of previous hemorrhage and destruction of tissue. Reestablishment of the circulation terminates menstruation.

The experimental bleeding which results from the types of hormone treatment previously described is similar to normal menstruation as regards amount, duration and local vascular phenomena. In spite of a vast amount of investigation relating to menstruation in general, little or nothing has been learned concerning the local mechanisms involved in the production of menstrual abnormalities. In 1941, our colleague, Dr. Rucker Cleveland,³ then of the Department of Anatomy, noted the occurrence of prolonged bleeding in castrated monkeys which had received estrogen and progesterone simultaneously, following an initial 14-day period of treatment with estrogen alone. As far as we have been able to find, this is the first reported instance of an experimentally produced menorrhagia. Doctor Cleveland's observation suggested a study of the vascular changes in the endometrium during this type of prolonged bleeding. Accordingly, intra-ocular endometrial transplants were made in four castrated monkeys. These animals were then injected with estrogen and progesterone, as in Doctor Cleveland's experiments. Vaginal bleeding of 15 to 23 days' duration followed cessation of treatment. During the first three to five days there was a profuse flow of red blood, subsequently, the flow was less profuse and the color was red at times but, on the whole, darker. The changes observed in the transplants were essentially similar to those described by Markee.² Hemorrhage was observed

only during the first day or so of vaginal bleeding, subsequently, the transplants remained anemic until shortly before or after the cessation of vaginal bleeding. At this time, restoration of the circulation and some regeneration of tissue were noted. These observations suggest that the initial breakdown of the tissue proceeded more or less on schedule and that the prolongation of bleeding was due primarily to delayed restoration of the circulation.*

This method of study, while it promises to give some insight into the mechanism of menorrhagia, does not afford any information concerning the central phase of the problem of menstrual disorders, nor concerning the changes in endometrial histology which are associated with abnormal bleeding. We have approached these phases of the problem from another angle, and the results of our studies have yielded information concerning the endocrine changes ultimately responsible for abnormalities of menstruation. The conclusions are of importance and rest upon the following experimental basis.

Our earlier experiments⁴ were undertaken in an attempt to obtain evidence concerning the etiology of glandular cystic hyperplasia of the endometrium. Castrated mice were injected with small daily doses of estrin and progesterin, singly and in combination. Their endometria were compared with human endometria, from the various phases of the cycle and with specimens of glandular cystic hyperplasia. The endometrial reactions of the estrin-treated mice and of the human endometria from the first 14 days of the cycle were identical, and, except for a lesser degree of proliferation and the absence of cystic glands, were similar to glandular cystic hyperplasia. This suggested that an increased estrogenic stimulus might produce hyperplasia. Accordingly, castrated guinea-pigs were injected with larger doses for a longer period of time. Typical glandular cystic hyperplasia resulted.⁵ In these animals, the vaginal smears showed a continuous estrous reaction. Just about this time, Haterius,⁶ and Emery,⁷ reported the occurrence of continuous estrus following extreme partial castration. The application of this procedure to the study of hyperplasia was obvious.

Meanwhile, we, and many others as well, were engaged in an attempt to correlate the disturbances of menstruation with endometrial changes. The endometrial biopsy technic which we introduced about this time^{8, 9} was of great help in the collection of the necessary data, which showed, conclusively, that any kind of a menstrual disturbance could arise from any kind of endometrium. Due to the fact that such opposite symptoms as amenorrhea and menorrhagia could both arise from the same type of endometrium, many competent observers referred different symptoms to different glands, and such terms as thyroid menorrhagia and pituitary amenorrhea were common. Some even thought that the association of a particular glandular lesion with a particular symptom was of primary diagnostic import. The results of our partial castration experiments¹⁰ shed considerable light on these points. Guinea-

* These experiments were supported by a grant from the S. E. Massengill Co. The hormones used (Progynon-B and Proluton) were kindly supplied by the Schering Corporation, through the courtesy of Drs. Erwin Schwenk and Bradley Whitman.

pigs were partially castrated and observed for 110 days. In some animals the estrous cycle continued normally, in a second group, there was continuous estrus and in another group estrus occurred infrequently or not at all. In the animals with normal cycles the ovaries showed small and infrequent corpora lutea and the endometria showed a fairly normal estrogenic stimulus but a deficient progesterone stimulus. In the group with long periods of estrus the ovaries were cystic and contained no corpora lutea. The endometria showed characteristic glandular cystic hyperplasia. In the animals with no cycles or infrequent estrus, the ovarian fragments were small and contained no corpora lutea and the endometria showed a deficient estrogenic stimulus and lack of any progesterone stimulus.

Thus, with experimental ovarian failure three different groups of individuals could be distinguished by changes in the sex cycles and endometria.

Studies of human endometria revealed that women with menstrual disorders could be classified in three similar groups, characterized, respectively, by (1) evidence of a deficient progesterone stimulus in the endometrium, corpus luteum in the ovary, (2) marked proliferation in the endometrium, no corpora lutea in the ovaries, and (3) minimal or no proliferation in the endometrium, ovaries atrophic. While there was no absolute correlation between the type of endometrial reaction and the type of menstrual disorder, there was a tendency for the milder types of menstrual disorders to be associated with endometrial reactions of the first type, excessive bleeding with those of the second type and amenorrhea with those of the third type. These observations led to the important conclusion that the various endometrial changes in these cases result from different degrees of ovarian failure. In general, three levels of ovarian failure can be distinguished. In the interest of simplicity we have designated them as the first, second and third degrees of ovarian failure. These are not static or sharply delimited conditions. Each merges gradually into the next and within each category there are variations in the level of ovarian activity.

With this picture of ovarian failure established, it was only natural to attempt the production of a similar picture by other means which would reduce the function of the ovary. Since hypophysectomy completely abolishes ovarian function it seemed logical to expect that partial hypophysectomy would produce a partial ovarian failure. Therefore, a number of guinea-pigs were partially hypophysectomized and observed for 110 days. These animals showed changes in the sex cycle and endometrium identical with those observed in the partial castration experiments.¹⁰

Under normal conditions sexual periodicity is dependent upon the proper adjustment of the hypophyseal-ovarian relationship. The above experimental results illustrate the fact that similar abnormalities in the genital tract can be produced by altering either component of the relationship. Clinical evidence indicates that a variety of other conditions, such as lesions of other glands or constitutional conditions or nutritional deficiencies, can alter the hypophyseal-ovarian relationship and produce changes in the genitalia. We

have some experimental evidence confirmatory of this supposition. In thyroidectomized animals the picture of ovarian failure is identical with that seen in the animals subjected to partial castration or partial hypophysectomy.¹¹ A somewhat similar picture has recently been observed in animals afflicted with a general constitutional disease, chronic cecitis. In animals with experimental hypertension resulting from partial nephrectomy, there was definite evidence of lowered ovarian function.¹²

Many investigators have obtained experimental evidence confirmatory of that described above. The production of glandular cystic hyperplasia by prolonged treatment with estrogen has been demonstrated in all of the common laboratory animals.¹³⁻¹⁷ Production of the typical endometrial picture in the macaque by this means has recently been reported from our own laboratory.¹⁸ The results of our partial castration experiments have been confirmed repeatedly.^{19, 20} The interesting experiments of Ranson, and his collaborators,²¹ on the effects of hypothalamic lesions are highly suggestive as to the mechanism of pituitary dysfunction. Abundant clinical evidence is also at hand which parallels the conclusions drawn from our experimental data. From all of the evidence, we have formulated the following general concept of menstrual disorders. To state it briefly:

Functional menstrual disorders result from an ovarian failure. This may be primary, due to inherent ovarian disease, or secondary, due to extra-ovarian causes, such as pituitary, thyroid or other endocrine disease and various types of constitutional disease. The approximate degree of ovarian involvement is indicated by the endometrium. There is no constant correlation between the primary lesion, the menstrual symptom and the endometrial reaction.

REFERENCES

- ¹ Allen, E. The Menstrual Cycle of the Monkey, *Macacus Rhesus*. Observations on Normal Animals. The Effects of Removal of the Ovaries and the Effects of Injections of Ovarian and Placental Extracts into the Spayed Animals. *Contrib Embryol* (No. 98), Carnegie Inst. Washington, 19, 1, 1927.
- ² Markee, J. E. Menstruation in Intra-ocular Endometrial Transplants in the Rhesus Monkey. *Contrib Embryol* (No. 177), Carnegie Inst. Washington, 28, 221, 1940.
- ³ Cleveland, R. Observations on Hormone-Withdrawal Bleeding in Castrated Macaques. *Endocrinol*, 29, 343, 1941.
- ⁴ Burch, John C., Williams, W. L., and Cunningham, R. S. The Etiology of Endometrial Hyperplasia. *Surg., Gynec., and Obstet.*, 53, 338, 1931.
- ⁵ Burch, John C., Wolfe, J. M., and Cunningham, R. S. Experiments on Endometrial Hyperplasia. *Endocrinol*, 16, 541, 1932.
- ⁶ Haterius, H. O. Vaginal Cornification and Ovarian Blood Supply. *Anat. Rec.*, 47, 318, 1930.
- ⁷ Emery, F. E. Changes in the Ovary and the Estrous Cycle Following the Removal of One Ovary in Albino Rats. *Physiol. Zool.*, 4, 101, 1931.
- ⁸ Burch, John C., and Klingler, H. H. Endometrial Biopsy by Suction. *Jour. Tennessee State Med. Assn.*, 25, 142, 1932.
- ⁹ Klingler, H. H., and Burch, John C. Suction in Obtaining Endometrial Biopsies. *J. A. M. A.*, 99, 559, 1932.

- ¹⁰ Burch, John C, McClellan, G S, Johnson, C D, and Ellison, E T The Diagnosis and Classification of Menstrual Disorders J A M A, 108, 96, 1937
- ¹¹ Williams, C, Phelps, Doris, and Burch, John C Observations on the Effect of Hypothyroidism on Ovarian Function in the Guinea-pig Endocrinol, 29, 373, 1941
- ¹² Diaz, J T Effect of Subtotal Nephrectomy upon Estrous Cycle of the Albino Rat Proc Soc Exper Biol and Med, 45, 226, 1940
- ¹³ Parkes, A S Experimental Endometrial Hyperplasia Lancet, 1, 485, 1935
- ¹⁴ Tietze, K Die Follikelpersistenz mit glandularer Hyperplasie des Endometriums in vergleichend pathologischer, experimenteller und genetischer Beziehung Ztschr f Geburtsh u Gynak, 108, 79, 1934
- ¹⁵ Zuckerman, S, and Morse, A H The Experimental Production of Excessive Endometrial Hyperplasia Surg, Gynec, and Obstet, 61, 15, 1935
- ¹⁶ Zuckerman, S Cystic Endometrial Hyperplasia in the Rhesus Monkey Jour Obstet and Gynec Brit Emp, 44, 494, 1937
- ¹⁷ Nelson, W O Endometrial and Myometrial Changes, Including Fibromyomatous Nodules, Induced in the Uterus of the Guinea-pig by the Prolonged Administration of Oestrogenic Hormones Anat Rec, 68, 99, 1937
- ¹⁸ Cleveland, R, Phelps, D, and Burch, John C The Experimental Production of Glandular Cystic Hyperplasia in Castrated Macaques Endocrinol, 28, 659, 1941
- ¹⁹ Lipschutz, A Hyperplasia experimentale de l'endometre avec proliferation atypique de l'epithelium uterin apres des interventions ovariennes Gynec et obset, 36, 408, 481, 1937, and 37, 17, 1938
- ²⁰ Schmidt, I G Changes in the Genital Tracts of Guinea-pigs Associated with Cystic and "Interstitial Gland" Ovaries of Long Duration Endocrinol, 24, 69, 1939
- ²¹ Dey, F L Changes in Ovaries and Uteri in Guinea-pigs with Hypothalamic Lesions Am Jour Anat, 69, 61, 1941

DISCUSSION—DR JOE VINCENT MEIGS (Boston) Doctor Burch has clearly described his interesting work and his interpretation of it There is no doubt that menstruation is a circulatory phenomenon, partially, but not wholly, controlled by ovarian hormones There is no doubt that the ovary, if normal, controls the normal endometrium of a normal uterus, but menstruation or bleeding from the endometrium may be under the control of the sympathetic nervous system or other nerve supply Also, the end-organ—the uterus and its endometrium—will respond differently depending upon its development, just as in the same individual the breasts, whose growth is under the control of the ovarian hormone, may respond to ovarian stimulation by growing to different sizes The reason for this is not that the ovarian hormone is supplied to each breast in varied amounts, but that each breast, as an end-organ responds differently to the same stimulation The underdeveloped uterus and endometrium, as end-organs, may respond poorly to normal amounts of hormones and bleeding may be very different from the bleeding of a well developed organ It is possible, also, that the response of the blood vessels and their nerve apparatus in individual organs may be abnormal Bleeding will be greater from an organ with a superior blood supply than from one with an inferior blood supply The fact that menstruation can be brought on suddenly or may stop because of fright or emotional shock shows that bleeding is not primarily controlled by ovarian hormones but is a nerve or blood vessel phenomenon, or possibly adrenal mechanism The normal ovary rules the normal endometrium and its normal blood supply, and an abnormal ovary with an abnormal secretion will pervert the bleeding from a normal uterus An abnormal physiologic state, such as pituitary failure, thyroid failure, starvation or disease will upset menstruation and may do so not because of partial ovarian failure, but because the end-organ and its blood vessels may be disorganized as well as the ovary The causes of normal menstruation are controlled by a normal ovary endometrium and blood vessel arrangement, but abnormal menstruation or bleeding or amenorrhea may be due to conditions far removed from ovarian failure Ovarian failure will upset menstruation but ovarian failure is not the only mechanism that can do it The most important link in the chain is the control of the neurovascular system If hormones control this system then hormone failure is most important, but if not, then a search must be made for another control

NEUROGENIC SHOCK

I THE EFFECTS OF PROLONGED LOWERING OF BLOOD PRESSURE BY CONTINUOUS STIMULATION OF THE CAROTID SINUS IN DOGS

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DURING THE PAST CENTURY AND A HALF, in which the word shock has been used medically to indicate a state of acute circulatory embarrassment or failure associated with wounds, hemorrhage and other accidents, there has existed a marked tendency on the part of the medical profession to consider it brought about somehow through the nervous system.

Psychic activity incident to the accident and resulting in the passage of impulses from the brain to the vasomotor centers in the medulla may play a variable rôle and may be difficult to evaluate. That vasodepressor centers exist in the cerebral cortex was shown recently by Hoff and Green¹ who produced a decline in blood pressure by electrical stimulation of the lateral suprasylvian, ectosylvian and sylvian gyri in cats and occasionally the marginal gyrus and a small area of cortex near the anterior tip of the superior precentral sulcus in monkeys. Fainting frequently accompanies a variety of sudden accidents and may send the blood pressure to very low levels.² If the reaction is marked and prolonged, as is rarely the case, and if combined with other shock-producing factors such as hemorrhage, it may be of importance in initiating or prolonging a state of shock. Fear has been considered by Freeman,³ Cannon,⁴ and others, to be an exciting factor in shock by increasing the output of adrenalin producing vasoconstriction with damage to and increase of permeability of capillaries, hemoconcentration, and secondary fall of blood pressure.

Injury to sensory nerves of the traumatized field resulting in afferent impulses to the vasomotor centers in the medulla is the method of action that has been most generally considered. The sensory stimuli are generally assumed to inhibit vasoconstrictor impulses and lower blood pressure although the possibility exists that vasodilator impulses may simultaneously be augmented. The most serious objection to this theory is that while vasodepressor responses may be elicited by electrical stimulation or by mechanical stimulation (as by cutting, pinching or stretching) of cerebro-spinal nerves during operations on man or experiments on animals, they are usually absent in most of these instances and if present are practically never of a degree that results in shock or even in marked and prolonged lowering of blood pressure.

The carotid sinus and cardio-aortic nerves are special afferent modulator nerves for the blood pressure with centers in the medulla and axonal endings in the walls of the blood vessels and in case of the cardiac division of the cardio-aortic nerve in the left heart. Stimulation of these nerves results in lowering of the blood pressure which varies to some extent in degree and duration with the nature, strength and length of the stimulus. The existence of similar modulator nerves has been postulated for other arteries, such as those of the abdomen, but never definitely proven. It has been the general observation that falls of blood pressure often to shock levels (70 Mm of mercury or under) may usually be produced within a period of one to three minutes by appropriate stimulation of either the carotid sinus or the cardio-aortic nerves. The pressure may be maintained at a low level for an indefinite period or it may rise to varying levels as a result of varying degrees of exhaustion of the reflex. However, no reports have been found in the literature of very prolonged stimulation of these nerves in an endeavor to determine whether or not the blood pressure can be maintained at low levels for a sufficiently long time to become the sole or an important factor in the causation of shock. Freeman³ lowered blood pressure in five cats by cardio-aortic nerve stimulation maintaining it between 60 and 80 Mm of mercury for 95 minutes in one case. The accompanying blood changes were negligible and the pressure promptly returned to the original level on removal of the stimulus.

Experiments have been conducted in an effort to determine the effect of continuous and prolonged stimulation of the carotid sinus of the dog and of the cardio-aortic nerves of the rabbit. Also, an attempt has been made to determine whether or not there are similar nerves supplying blood vessels within the abdomen which on stimulation lower the blood pressure. The results of carotid sinus stimulation are reported here.

The vasodepressor effect of stimulation of the carotid sinus was discovered by Heering,⁵ and Koch,⁶ and has since been considerably elaborated by Heymans and coworkers,⁷ and others. Short to medium periods of stimulation in dogs have not been found to bring on a state of shock although sudden reflex death has occasionally resulted during dissection or mechanical or electrical stimulation of the carotid sinus or its nerve.

EXPERIMENTAL METHODS

Dogs weighing from 7 to 15 Kg were anesthetized with sodium barbital, 300 mg per Kg body-weight, intravenously. When smaller doses were tried there was usually struggling and disruption of the set-up especially on electrical stimulation. The experiment was also set up under evipal anesthesia, and the animal allowed to recover. Stimulation then also produced struggling and disruption of the set-up. Kymographic tracings of blood pressure were recorded from a cannula in the femoral artery. Stimulation was produced in some cases mechanically by distention of the carotid sinus, in others electrically by an induced current passing through a bipolar elec-

trode applied to the sinus in one form externally and in another form intravascularly. Erythrocyte counts, hematocrit, and in some cases hemoglobin and serum protein determinations, by the Barber-Hamilton method, were made before and at intervals in the course of the stimulation. Blood was drawn from the exposed femoral vein in most experiments but more recently from the femoral artery.

Mechanical Stimulation—For mechanical stimulation the technic of Heymans was used. An inverted jugular vein sac was attached to the end of a cannula which was then inserted and tied in the carotid artery, so that the sac rested in the sinus. The external carotid artery was ligated near its origin. By distention of the sac with water the pressure was raised to the desired levels. Sac pressures ranging between 175 and 275 Mm. of mercury were found to give the greatest falls in blood pressure.

There were eight experiments of this kind. Sinus distention promptly lowered the blood pressure to some degree in seven but in only three did the level reach 70 Mm. of mercury or lower. Usually, regardless of the level of descent the pressure began to rise within a few minutes and reached the previous level in from 10 to 40 minutes. After periods of rest there would usually be a response to stimulation of the same character. One dog which showed falls of blood pressure of 20 to 40 Mm. lasting up to 30 minutes, died suddenly when the pressure was released at 120 Mm. mercury. In one dog there was failure of response despite repeated and varied elevations of pressure in the sinus. Section of the vagi in three cases after failure to hold the pressure at low levels by stimulation made little difference in results. The remaining animals were sacrificed after 4 to 13 hours while stimulation was not being carried out. Their blood pressures were at or only slightly below the levels before stimulation was begun and there were no changes in R. B. C. counts or hematocrits, or other evidences to indicate a state of impending or existing shock. The method of stimulation was consequently abandoned as being inadequate.

Electrical Stimulation with Electrode Applied Externally—In a second group of 14 experiments the region of bifurcation of the common carotid artery was dissected free of surrounding soft parts. One wire of a bipolar electrode was hooked about the internal carotid and the other about the common carotid near the bifurcation. In addition, five animals died suddenly during the dissection in an attempt to carry out this procedure, from reflex respiratory and/or cardiac arrest, it being difficult to say which.

Stimulation was from a Harvard inductorium with 6 to 11 cm. separation of the secondary coil from the zero point. Leakage of current to the surrounding soft parts was troublesome. In 10 experiments there were falls of blood pressure but the degree and duration were very variable. Five animals showed moderate short responses but died suddenly at the onset or within 12 minutes to 2 hours in the course of stimulation, probably from current leakage to the adjacent vagus. Only two dogs had prolonged falls of pressure.

In one, the initial pressure was 150 Mm, and under almost continuous stimulation for 6 hours it ranged between 80 and 100 Mm and the erythrocytes increased gradually from 6,480,000 to 8,020,000, and the hematocrit from 53 to 59. Death occurred suddenly from vagus arrest of the heart. In a second dog the pressure fell initially from 145 Mm and fluctuated between 75 and 125 Mm under continuous stimulation for 11 hours. When the stimulus was removed for $\frac{1}{2}$ to 2 minutes, the pressure always bounded upward to 140–160 Mm and when released at the end, before killing, it was 155 Mm. The erythrocytes were 6,080,000 and the hematocrit 43 before stimulation. After $5\frac{1}{2}$ hours they were 6,800,000 and 48, respectively. Estimations 10 minutes before the stimulus was stopped showed 12,000,000 erythrocytes (inaccurate?) and a hematocrit of 60. Thus, despite the fact that the stimulus was removed after 11 hours, the blood pressure rose as high as it was at the beginning, showing that vasomotor control was still normal. Hemoconcentration had developed during the last 4 hours.

Electrical Stimulation with a Cannula Electrode—In an endeavor to improve the method of stimulation, a bipolar cannula electrode was devised. It is inserted and tied in the common carotid artery, the distal pole being carried into the first portion of the internal carotid leaving the proximal pole in the carotid sinus. The cannula and the method of insertion are shown in Figure 1. For the prevention of leakage of current, the carotid artery is tied and divided proximally, the freed surrounding soft parts retracted by two Farr automatic retractors and one ribbon retractor anchored to a cross bar. The set-up of the experiment is shown in Figure 2. In four experiments, both carotids were cannulated but the results of bilateral stimulation were little different from those of unilateral stimulation.

The results of cannula electrode stimulation in 19 experiments were a great improvement over those obtained by previous methods, as the circulation of the sinus was well preserved, and it responded to stimulation for long periods. By avoiding dissection about the carotid sinus nerve, there was no death during the preparation of the experiments. In every experiment there was at some time a response to stimulation but there was variation in the intensity, duration and time at which it was obtained. With initial blood pressures varying from 110 to 160 Mm mercury, there was usually a fall at the onset of stimulation with the secondary coil 10 to 8 cm from the zero point. In the majority of the experiments the pressure fell from 25 to 50 Mm of mercury, leaving it at suprashock levels and sometimes much stronger stimuli were necessary. However in a minority of cases the fall was to 70 Mm of mercury, or lower. The most marked falls were usually in animals showing little or no embarrassment of respiration. In experiments giving the most marked and persistent response it was possible to lower the blood pressure to shock levels either immediately or relatively soon after the onset of stimulation and maintain

TABLE I
CAROTID SINUS STIMULATION MAINTAINING BLOOD PRESSURE ALMOST CONTINUOUSLY
AT SHOCK LEVELS UNTIL DEATH

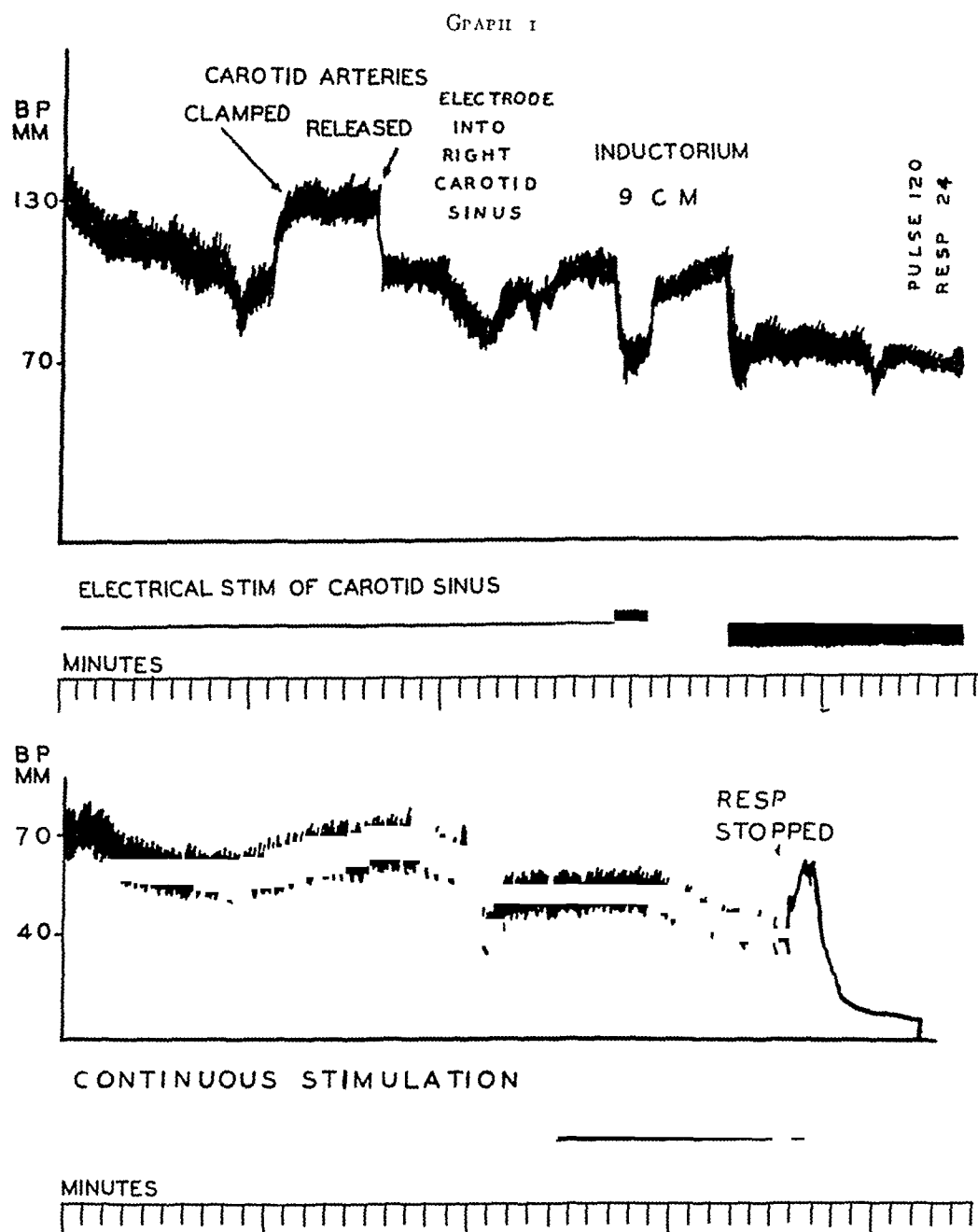
Exper No	Survival Hours	Stimu lation Period Hours	B P Mm Hg	Pulse Rate	Res pira tion	R B C Millions	Hemat ocrit %	Pathology
114	7 5	0	110	120	20	7 14	48	Lung Congestion of capillaries and venules little hemorrhage and protein precipitate in alveoli Liver Extreme stasis in both hepatic and portal systems Liver cords either vacuolated or granulated in places Some lymphatics markedly distended with lymph coagulum Kidneys Marked congestion and acute granular degeneration of epithelium of tubules Adrenals Marked congestion some hemorrhage and degeneration of cells of fasciculate zone Little cortical and medullary change Lymphatic ganglion near adrenal Extensive degeneration of nuclei of some cells Changes in other viscera negligible
		0 1	66					
		1 0	60	124	24	7 14	47	
		2 0	50	142	20	7 52	51	
		3 5	70	138	28	8 72	57	
		5 5	70	134	22	9 60	61	
119	9 5	7 5	35			9 14	59	
		0	130	120	16	5 44	57	
		0 2	76					
		1 0	100	116	22	7 28	40	
		2 5	74					
		3 5	83	96	8	7 12	40	
129	8	6 5	65	84	8	6 88	39	
		9 25	41	152	7	6 08	39	
		0	106	126	36	5 28	33	Necropsy Moderate edema and atelectasis of lungs Aspirated vomitus in some bronchi Central congestion and slight granular degeneration in cords of liver lobules Slight degeneration of fasciculate zone of adrenal cortex Nuclear degeneration in convoluted tubules of kidneys Spleen small and anemic as in collapse Other visceral changes negligible
		0 1	50					
		1 0	74	120	20	5 76	30	
		3 0	70	140	28	7 56	39	
		6 25	75	136	26	7 36	36	
		7 75	44	144	48			

Average 8 3

it continuously or almost at such levels until circulatory exhaustion and death occurred. A summary of the results of three experiments is given in Table I.

The average survival time after beginning the continuous stimulation was 8.3 hours. As the blood pressure gradually declined there was a tendency to hemoconcentration as shown by the erythrocyte counts and the hematocrit. This was slight in Experiments 119 and 129. Necropsy in Experiments 114 and 129 revealed congestion and acute degenerative changes in most of the viscera. The hemoconcentration and pathologic changes were most marked in Experiment 114, in which the blood pressure was most consistently at low levels, and in which death occurred earliest after 7.5 hours. Graph 1 shows the early blood pressure tracing with the rise and fall of pressure from clamping and releasing the common carotid arteries, the fall of pressure from short stimulation with the inductorium at 9 cm. and the early part of the prolonged period of continuous stimulation. Release of the stimulus for 2 minutes three hours after the beginning with a pressure of 62 Mm. of mercury resulted in a rise of 30 Mm. However, a similar release 55 minutes before death resulted in only an 8 Mm. rise in pressure, showing that the circulation was so badly damaged that an almost irreversible

state was present. Graph 2 shows the further decline during the final 35 minutes of life. Photomicrographs show the blood and lymph stasis in the liver (Fig 3), the cell necrosis in the convoluted tubules of the kidney (Fig 4) and the disappearance of nuclei in sympathetic ganglion cells (Fig 5).



GRAPH 1—Experiment 114. Showing carotid sinus reflex from clamping and releasing carotid arteries and electrical stimulation of right carotid sinus.

GRAPH 2—Experiment 114. Blood pressure tracing before death, following $7\frac{1}{2}$ hours of stimulation, with maintenance at shock levels.

In the larger group of experiments in which for a long period, the reduction in blood pressure was to irregular suprashock levels, the general effect on the animals was relatively slight, and on release of the stimulus the pressure would mount to approximately the prestimulation levels. At times

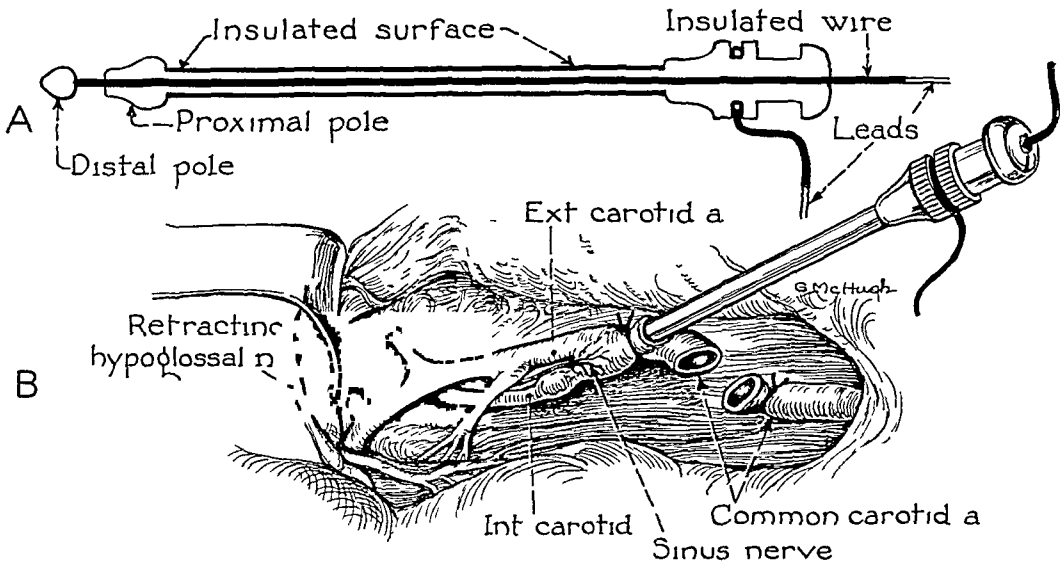


FIG 1—A Insulated bipolar cannula electrode B Electrode inserted through right carotid artery with distal pole in internal carotid artery and proximal in carotid sinus

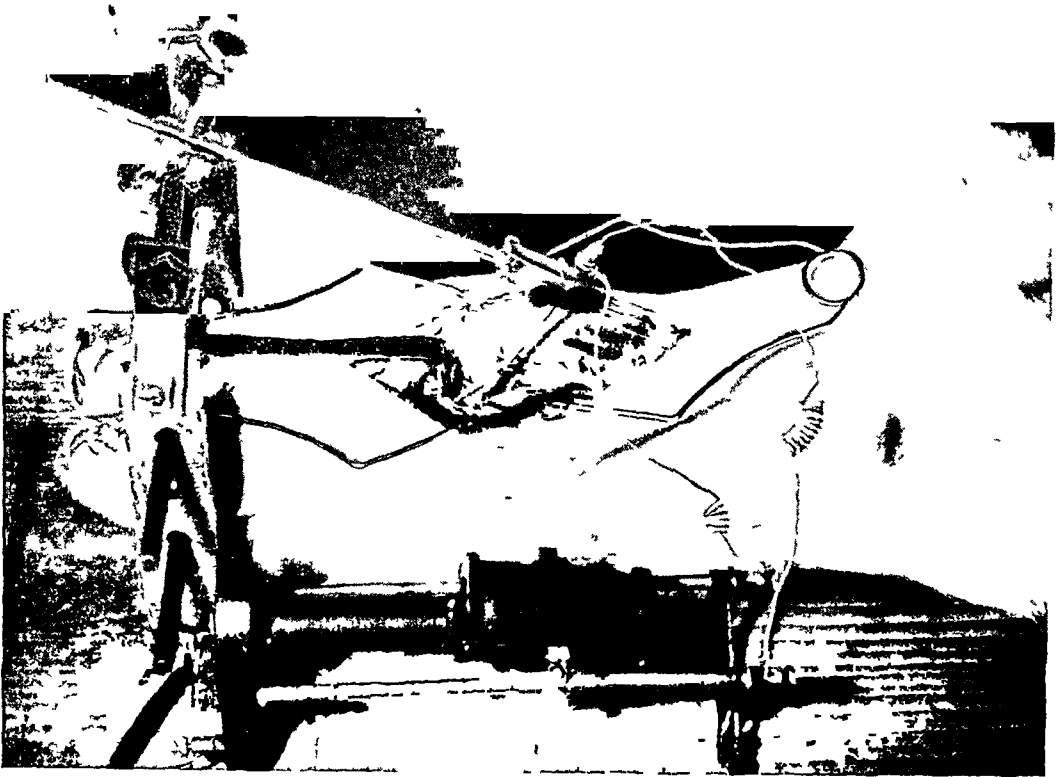


FIG 2—Experiment set up for stimulation Cannula inserted in carotid sinus and held in the clear by clamp Surrounding soft parts retracted by one anchored ribbon retractor and two Farr automatic retractors

the reflex would be exhausted and the pressure would rise to previous levels Following a brief rest period, the pressure would again fall on stimulation

TABLE II
BLOOD PRESSURE LOWERED TO SUPRASHOCK LEVELS DURING ABOUT THE
FIRST TWO-THIRDS OF PERIOD OF CAROTID SINUS STIMULATION

Exper No	Survival Hours	B P		Pulse Rate	Resp Rate	Hemato-		Pathology
		Time Hours	Mm Hg			R B C Millions	crit %	
131	26	0	120	138	16	6 96	35	Operative wounds infected Marked hypo- static congestion of lungs Some blood in alveoli Lymphatics distended with co- agulum Central venous engorgement in liver with degeneration in adjacent cords Some degeneration in cortical zone and de- generation and hyperemia in fascicular zone of adrenals Extensive degeneration and sloughing of convoluted tubules of kidney Moderate hyperemia of kidney and spleen Subepicardial vascular engorge- ment with lymphatics distended by lymph coagulum Slight waxy degeneration of myocardium Pancreas, jejunum and skeletal muscle normal Some degeneration in peripancreatic sympathetic ganglion
		0 3	80					
		0 6	80	128	20	5 52	31	
		1 6	90	136	20	5 78	35	
		2 6	100	168	20	5 48	34	
		5 0	84	162	28	4 32	26	
		9 0	82	176	26	3 84		
		13 0	80	150	36	5 68	35	
		(over night)						
		22 5	72	172	28	6 4	39	
		24 6	68	170	28	6 24	40	
		25 6	45			5 59	41	
132	14 75	0	170	180	22	9 04	48	Operative wounds infected Hypostatic congestion and beginning pneumonia in posterior lobe of lung Passive congestion of liver and degeneration of cord cells Acute necrosis of cells of convoluted tubules and marked congestion of kidney Congestion and moderate degeneration in intermediary zone of the adrenals Pan- creas spleen jejunum and skeletal muscle normal Some fragmentation of myocardial fibers
		0 1	140					
		1 0	140	168	20	8 96	55	
		1 2						
		1 65	128					
		3 0	135					
		4 0	85	160	24	9 76	51	
		6 5	90	180	16	10 38	53	
		9 0	90					
		9 5	90	184	28	9 68		
		10 0	70					
		13 0	54	160	24	9 14	51	
133	18 3	0	130	138	24	6 90	47	Operative wounds infected Hypostatic congestion and slight atelectasis of lungs Engorgement of central lobe veins and necrosis of cords of liver Slight hyperemia and necrosis of tubules of kidney Moder- ate hyperemia necrosis and leukocytic infiltration of intermediary zone of adrenals Other viscera and cardiac muscle essential- ly normal
		0 25	90					
		1 0	98					
		2 0	100	160	28	8 00	51	
		4 5	115	168	32	7 44	45	
		9 0	110	176	19	6 56	44	
		9 75	105					
		11 5	80			8 40	44	
		15 5	70	144	24			
		16 5	60	144	32	7 28	46	
		18 0	20	160	16	6 72	42	

Average 19 7

However, after 10 to 20 hours of continuous, or almost continuous stimula-
tion, the blood pressure would decline to shock levels and then death would
result in a shorter time than in the animals whose pressures fell to shock
levels at the onset of the stimulation The results of three experiments are
given in Table II

The average survival period was 19 7 hours There was relatively little
fluctuation in the erythrocyte counts and hematocrit, either before or after
the blood pressure descended to shock levels The experiments ran long
enough for wound infection to be established and to play a part in the
causation of death

FIG 3

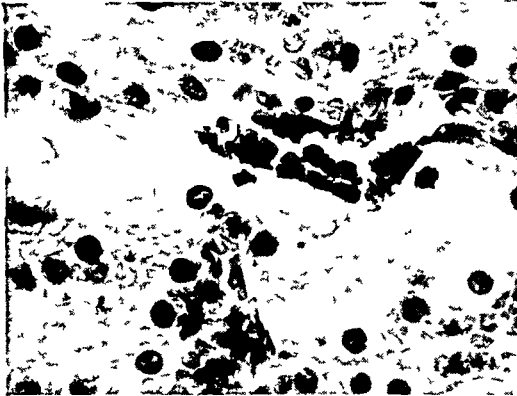
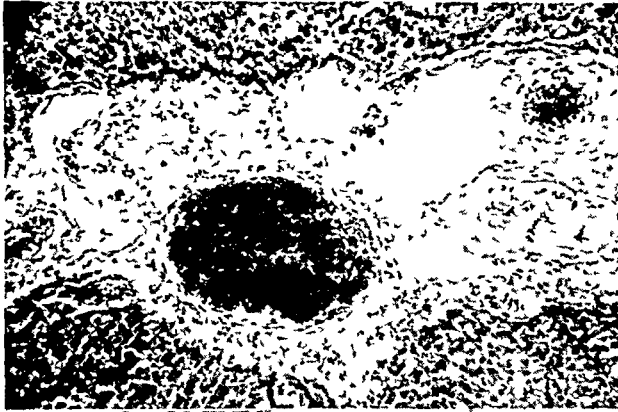


FIG 4

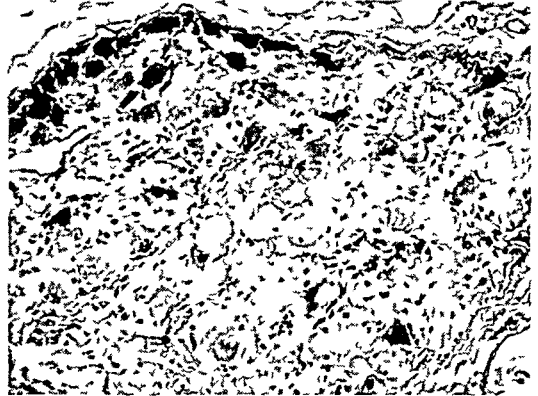
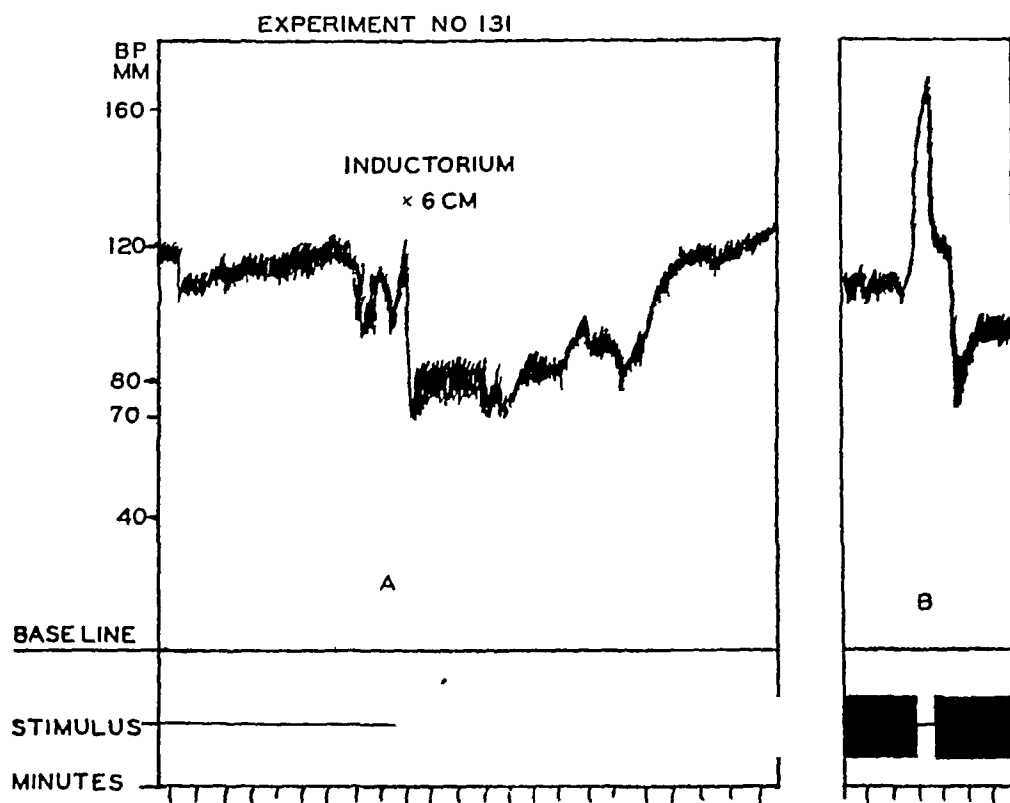


FIG 5

- FIG 3—Experiment 114 Engorgement of veins and capillaries with blood, and of lymphatics with lymph coagulum
FIG 4—Experiment 114 Necrosis of cells of kidney tubules
FIG 5—Experiment 114 Necrosis of cells of sympathetic ganglion

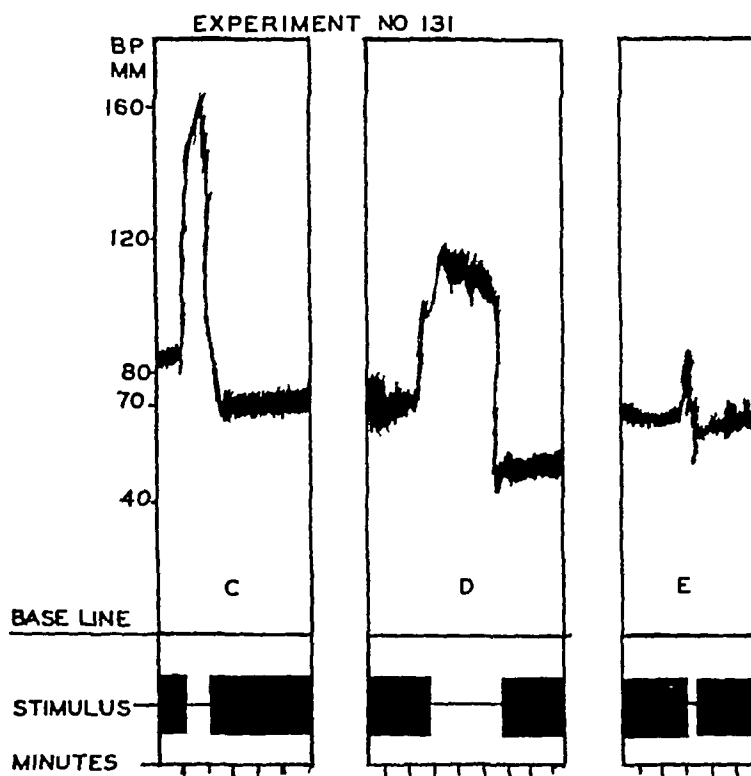
In Experiment 131 the animal lived 26 hours. The duration and degree of fall during the first 13 hours varied considerably. Graph 3 shows the decline of pressure on initial stimulation with the inductorium at 6 cm and the rapid return to a higher level despite continuation of the stimulus. After moving the secondary coil to 4 cm the pressure again fell and with that strength unchanged it remained at irregularly low levels until death. During the long period that the pressure remained at suprashock levels the rise of pressure on temporary release of the stimulus was very marked as shown at the end of 3.2 hours by Graph 3b, and at the end of 11.3 hours and 22.5 hours as shown by Graph 4c and d, respectively. However, after the pressure had been at shock levels for one hour, the elevation of pressure on release was very slight (Graph 4e) and after another hour it failed to occur.

For comparison with these two groups of stimulation experiments, a third or control group was run in which the procedure was the same except the electrical stimulus was not applied to the sinus. The results are shown in Table III. The average duration of life was 28.7 hours. The blood pressure did not drop to shock levels until an average of about 4 hours before



A - ONSET OF STIMULATION REFLEX QUICKLY EXHAUSTED
B - 40 SEC RELEASE AFTER 3 2 HRS CONTINUOUS STIM

GRAPH 3—Experiment 131 A Showing fall in blood pressure to suprashock levels with recovery during carotid sinus stimulation B Elevation of blood pressure on release of stimulus, while pressure is maintained at suprashock level for 3 2 hours



C - 45 SEC RELEASE AFTER 11 3 HRS CONTINUOUS STIM
D - 3 MIN " " 22 5 " " "
E - 20 SEC. " " 23 5 " " "

GRAPH 4—Experiment 131 Showing marked pressor response on release of stimulus after maintenance at suprashock levels for (C) 11 3/4 hours Response still good when shock level reached (D) after 22 1/2 hours, but feeble (E) after 23 1/2 hours

TABLE III
CONTROL EXPERIMENTS FOR CAROTID SINUS STIMULATION

Exper No	Survival Hours	Time Hours	B P Mm Hg	Pulse Rate	Respiration	R B C Millions	Hemato crit %	Serum Proteins	Pathology
134	26 35	0	145	88	28	9 60	56	5 61	Necropsy Early infection of wounds
		2 3	150	180	24	9 12	60	5 48	Early pneumonia
		8	150	205	24	10 24	60	5 78	Early necrosis of many cells of convoluted and collecting tubules of kidneys
		10 25 (over night)	140			10 32	57	5 61	Central congestion of liver lobules degeneration of liver cells
		22	80	88	12	8 72	53	5 48	Degeneration and nuclear fragmentation of adrenal cortex
		24	70	138	20	8 88	54	5 48	Slight waxy degeneration of heart muscles
		26	40			8 80	52	5 65	Other viscera and skeletal muscle showed no changes
135	31	0	160	180	22	7 76	51	5 58	Necropsy Moderate atelectasis and congestion of lungs
		2	160	180	20	7 84	53	6 26	Degeneration of glomerular zone and of cells of cords of adrenal cortex
		8	160	180	20	8 64	54	6 35	Slight degeneration and sloughing of cells of convoluted tubules of kidney
		14	130	170	28	8 08	50	6 22	Congestion of liver lobules
		20	90	144	10	8 16	52	5 65	Other viscera show no change
		25	70	150	12	7 68	49	under 5 58	Infection of wounds
		30	50	164	10	6 90	48	under 5 58	
187	29	0	120	144	24	5 68	45		Hb 84 Hypostatic congestion of lungs and early pneumonia
		1 6	110	140	40	6 08	47	5 31	86 Necrosis of cells of tubules of kidneys
		4	126	160	44	5 84	50	5 48	85 Hyperemia
		8	120	180	44	6 80	49		92 Necrosis and leukocytic infiltration of intermediary zone of adrenal
		12 (over night)	100	180	48	6 94	49	5 48	96 Marked engorgement of liver veins and necrosis and leukocytic infiltration of liver cells
		20	86	190	36	7 20	49	5 24	102 Other viscera and skeletal muscle show negligible change
		24	80	180	54	7 68	49	4 97	104 Infection of experimental wounds
		28	60	160	88	6 72	47	5 24	95

Average 28 7

death. There was no significant change in the erythrocyte counts, hematocrit or plasma proteins. Infection of the operative wounds was more marked than in the group of cases represented in Table II.

DISCUSSION.—The factors to be considered in the causation of death of the animals in which the carotid sinus was stimulated electrically, with the use of the bipolar cannula electrode, are the effects of the stimulus, the anesthetic, the experimental wounds, and the possible late complications from infection and dehydration.

In the group of animals represented in Table I, in which the blood pressure was maintained at shock levels during nearly all of the period of stimulation, there was death after an average of 8.3 hours, with a tendency to hemoconcentration, which was marked in one case and slight in the other two cases. In the two necropsied cases there were acute congestive and degenerative changes in the cells of parenchymatous organs compatible with changes resulting from low blood pressure and failure of the circulation. The anesthetic produced sound narcosis, but there was no evidence that it was an important factor in the cause of early death. The experimental wounds were made with very little blood-loss, and death occurred before there was time for the appearance of toxic effects of their infection. Consequently, it

appears justifiable to conclude that the prolonged maintenance of the blood pressure near or below 70 Mm of mercury was the most important factor in the production of death from acute circulatory failure

In the group of animals represented in Table II, in which, during continuous or almost continuous stimulation, the blood pressure remained depressed but at irregular levels, above 70 Mm of mercury, the animals did not present a tendency to hemoconcentration, and on temporary release of the stimulus, the blood pressure quickly rose to high levels over a period of 10 to 20 hours. Finally, the blood pressure sank to 70 Mm or below, after which the animals died in an average of four to five hours showing a slight tendency to hemoconcentration during the period. Infection, prolonged anesthesia, and dehydration appeared to be the most important lethal agents and circulatory damage from lowering of blood pressure to suprashock levels by sinus stimulation was of much less significance

In the third group of control experiments, which lived on an average of 28.7 hours, the prolonged anesthesia and infection of the wounds, and of the respiratory tract were the factors of greatest importance in causing death. The blood showed little change, with a slight tendency to hemodilution, and the blood pressure fell to low levels late in the course of the experiments

SUMMARY

By electrical stimulation of the carotid sinus in dogs under sodium barbital anesthesia using a bipolar cannula electrode, it was possible to maintain the blood pressure at reduced levels for long periods of time and to observe the effects of the lowered blood pressure upon the body and the general circulation

In one set of experiments, in which the pressure was held continuously or nearly so at 70 Mm of mercury or below, the blood became concentrated and death occurred after the lapse of an average of 8.5 hours. At necropsy, there was congestion and acute necrosis of the cells of many of the viscera, and the picture was compatible with shock produced principally by the vasodepressor nerve stimulation

In a second set of experiments, in which the pressure was lowered by stimulation but remained above 70 Mm of mercury, there was relatively little damage to the circulation for many hours, as revealed by the absence of hemoconcentration and by prompt elevation of the pressure on temporary release of the stimulus. Finally, the pressures fell to shock levels, and death then followed in 4 to 5 hours with a total survival period averaging 19 hours. The anesthetic and the infections of the wounds and of the respiratory tract were important factors in the causation of death. However, that death was hastened by the blood pressure lowering effects of the stimulation is indicated by the fact that a set of control animals lived an average of 28.7 hours, or 9 hours longer than those of the second group, dying mainly from the effects of anesthesia and infection

While neurogenic shock has been produced by carotid sinus stimulation

in anesthetized dogs it has only indirect bearing on human shock, since similar stimulation would scarcely be encountered as a result of injury or during operation in man

The pathology of the experiments has been kindly reviewed by Dr Eleanor Humphreys

REFERENCES

- ¹ Hoff, E C, and Green, H D Cardiovascular Reactions Induced by Electrical Stimulation of the Cerebral Cortex Amer Jour of Phys, 117, 411, 1936
- ² Phemister, D B, and Livingstone, H Primary Shock ANNALS OF SURGERY, 100, 714, 1934
- ³ Freeman, N E Mechanism and Management of Surgical Shock Penn Med Journ, 42, 1449-1452 1939 *Idem* Decrease in Blood Volume after Prolonging Hyperactivity of the Sympathetic Nervous System Amer Jour of Physiology, 103, 185, 1933
- ⁴ Cannon, Walter B A Consideration of Possible Toxic and Nervous Factors in the Production of Traumatic Shock ANNALS OF SURGERY, 100, 704-713, 1934
- ⁵ Hering, H E Wien med Wchnschr, 73, No 16, 729, 1923
- ⁶ Koch, E Munchen med Wchnschr, 70, 1316, 1923 *Idem, ibid*, 71, 704, 1924
- ⁷ Hevman, C, Bouckaert, J J, and Regniers, C Le sinus Carotidien et la Zone Homologue Cardioaortique G Doin et Cie, Paris, 1933

THE STADER REDUCTION SPLINT

FOR TREATING FRACTURES OF THE SHAFTS OF THE LONG BONES

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IN 1931, one of the authors (Stader^{4, 5, 6, 7}) working in the field of veterinary surgery, was impressed with the inadequate methods then in vogue for treating fractures of the shafts of the long bones in dogs. Plaster encasements were not tolerated by the canines, who frequently destroyed them by constant biting and tearing, or the plaster disintegrated by constant soiling and softening with body excretions. Traction and counter-traction were obviously unsuited and although a modified Thomas splint had been used extensively, the degree of fixation obtained was usually insufficient and pressure necrosis from the ring often defeated its continued use. It was thus that Stader, using two half-pin units in each fragment, bridged by a metal adjustable connecting bar, was able to accurately reduce the fracture and allow the apparatus to remain in place and act as a splint. Anatomic reduction could usually be obtained by means of the adjustment on the splint, and because of its compact size it did not seem to annoy the dog and was well tolerated by the animal until union of the fracture had occurred.

In the human, Schanz^{1, 3} had described the use of half-nails and screws as a means of skeletal control, and Riedel² had suggested an external plate bridging two or more screws or nails, thus permitting firmer fixation. These authors further pointed out the advantages obtained in inserting the pins at an angle to each other (not parallel) as a means of firmer control over the bone fragments. Anderson made use of this principle in his work. Until 1931, all of these men finally fixed the pin assembly in plaster, incorporated as a circular plaster encasement.

Stader gradually used his splint in dogs with greater and greater frequency, and up to the present time (May, 1942) over 1200 fractures in dogs have been treated by this method. The results obtained have been uniformly good and far superior to the older methods of treatment.

In 1937, the two other authors of this paper (Lewis and Breidenbach) had the opportunity of seeing the application of the Stader splint in a police dog with a fractured shaft of the femur. The ease of application, the prompt and accurate reduction obtained, and the simplicity of the instrument made a distinct impression. In addition, the fact that the apparatus would act

as a splint during the ensuing weeks while union was taking place, seemed a decided advantage

It was then decided to have a larger model of the splint manufactured for use in the human. This was done and, in October, 1937, the first patient was treated by this method on the Fourth Surgical Division of Bellevue Hospital. The patient, W W, had a fracture of both bones of the leg, and after application of the splint he was bearing weight on the injured limb in two weeks, and walking without the aid of crutches or cane in three weeks. Impressed by the ease of reduction and the possibilities of early weight-bearing without immobilizing either of the adjacent joints, further trial of the splint in fractures of the shafts of the long bones in the human was carried out. Since 1937, a total of 20 patients have been treated by this method. The results have been uniformly good, except in three patients where infection around one or more of the pins occurred. In these cases the infection promptly subsided when the pins were removed. No osteomyelitis has been observed, except in the femur case described below, although in some patients the apparatus has been on for from 14 to 16 weeks. It has been our custom to keep the splint on until bony union has occurred, and this has varied from 8 to 16 weeks. Most of the cases have been fractures of the shafts of both bones of the leg (tibia and fibula), as will be seen in Table I. One fracture of the shaft of the femur was treated in an old man of 84. This case unfortunately succumbed, and because of the patient's age should not have been selected for a trial of the method. Some seepage around the pins, appearing between the 4th and 6th weeks, and due to galvanism between the bone and pin has been seen. This has been largely overcome since the pin bar has been made of a plastic instead of a metal. When it does occur, however, it is not of significance and promptly subsides after the splint and accompanying pins have been removed at the end of treatment.

DESCRIPTION OF MECHANICAL PARTS AND FEATURES OF THE STADER REDUCTION SPLINT

The mechanical features of the reduction splints are detailed in Plate I, Figures 1 and 2.

The stainless steel pins (A) are made of a special alloy which is resistant to corrosion when embedded in tissue. These pins have been permitted to remain *in situ* for as long as nine months, and upon removal were found completely free from any corrosion. The sharpened end is similar to the end of a trocar, while at the other end, there is a flat surface for the set screw of the pin handle.

In the procedure of applying the instrument, the pins are placed through the desired holes in the pin bar (B) and locked by means of a set screw (C). There are four holes (K) in each pin bar—the two extra ones being for the purpose of selection.

If there is a short fragment on one end of the fracture, it may be necessary to use the two pin holes nearest to each other, while on the long fragments, the pin holes farther away from each other may be desired. The two pins, when inserted through the pin bars, form an angle, and it is by this means that a definite contact is established to the bone. One of the pin assemblies (pin and bar) is placed above the fracture and another below the fracture.

These two pin bars are then abridged by the extension bar by means of the hinge bolts (D) being inserted through the large central hole in the pin bar and tightened by means of nuts (E). In order to overcome overriding of the fragments, the extension bar (F), which is in effect a turnbuckle, is activated by a wrench in such a manner as to cause the pin bars to travel away from each other.

By manipulation of the screws (H) which contact the pin bar from above, accurate alignment of the fragments in the mediolateral plane can be accomplished. Nut (E) should be slightly loosened before the adjustment is made.

By manipulation of the screw (I) each pin bar assembly and fragment can be accurately aligned in the anteroposterior relationship.

By activating the above mentioned adjustments, each fragment can be manipulated in each and every plane.

After the adjustments have been completed and checked roentgenologically, the lock nuts (G) on the extension bar are tightened firmly against the hinge block (L). This locks the instrument for both extension and rotation. The nuts (E) on the hinge bolt (D) are now firmly tightened and then the set screws (I) are firmly set, which locks the remainder of the instrument. The reduction instrument now assumes the rôle of a splint.

In order to reduce the weight of the instruments, most of the parts are made of duralumin, those parts absorbing great strain are made of stainless steel.

Before going into the detail of surgical procedure, it might be well to take up a few general considerations, in order to picture to the reader a few of the fundamentals in the use of the Stader reduction splint. If one refers to Plate I, Figures 1 and 2, it will be seen that the pin assemblies are placed as near the extremities of the bone as possible. This is exceedingly important and should be constantly kept in mind. The reasons for placing the pin assemblies close to the bone extremities are

1. The first principle in treating a fracture of the shaft of the bone is to correct the overriding. Overriding is caused by muscular contraction. As the muscles causing the overriding, for the most part, have their origin and insertion at or near the bone extremities it seems logical to inactivate them at these points. When these muscles are inactivated in this manner they cannot produce unusual strains upon the instrument or the bone fragments which they control.

2 Some of the serious objections to placing the pin near the point of fracture are

(a) They are introduced into the traumatized tissue which is devitalized in many instances

(b) When the pin assemblies are placed close to the point of fracture the muscle groups have a greater purchase upon the fracture bone fragments, by virtue of the fulcrum produced by the instrument. This, then, throws greater stress upon both the instrument and the fractured bone. In other words, one tends to hold the fracture in place by brute force.

(c) When the pin assemblies are placed close to the fracture it is more difficult to successfully reduce the fracture because of the previously mentioned muscular action upon the extremities of the bones.

The following mental conception of the problem may be useful. Normally an unfractured bone is situated in a muscular furrow. Now, by applying the apparatus near the extremity of the bone fragments, the fragments tend to float within this furrow during the reduction maneuvers. In this way all forces under extension tend to assist in reducing the fracture.

ACTUAL SURGICAL PROCEDURE OF APPLYING THE STADER REDUCTION SPLINT

Careful skin preparation is essential, and the same surgical aseptic safeguards should be observed as in any surgical procedure on bones. The splint should only be applied in the operating room, and careful sterilization is of course necessary.

Placement of the Pins—As a general rule the upper pin assembly is placed first. Place one of the pins into the pin handle or in a flexible shaft drill and tighten it firmly into place with the set screw. Introduce this pin through the desired hole in the pin bar and then hold this assembly in the right hand. With the left hand, accurately determine the point for pin No. 1 to enter. Steadying the area with the skin stretched toward the fracture by the left hand, the right hand introduces the pin and by firm, steady pressure forces the pin through the skin and soft tissues on to the outer cortex of the upper fragment of the bone.

By firm pressure and rotation, the pin is firmly seated into the outer cortex. Then, by deep palpation upon the medial side of the limb the upper fragment is steadied while the pin bar is brought into *parallel alignment* with the long axis of the upper fragment by means of slightly altering, if necessary, the angle of introduction of the pin which up to this point has only been seated. After the upper fragment and pin bar have been brought into parallel alignment, continued pressure and rotation of the pin handle will introduce the pin through the outer cortex, through the medullary canal and then through the inner cortex. Care should be exercised so that the pin-points definitely emerge through the inner cortex. This can be ascertained by a gradual release of resistance as the pin points start to emerge,

as well as by deep digital palpation which will frequently reveal the pin-points through the inner cortex

The insertion of the pins is difficult in some instances, especially so where the cortex of the bone is unusually thick. If this difficulty is met with, drilling a hole with a bone drill slightly less in diameter than the pins to be used, will overcome the problem. The pin is then introduced through the tract of the drill, after the drill has been withdrawn.

When using a drill it must be passed through the pin block in order that the hole being drilled will assume the proper angle. The drill should

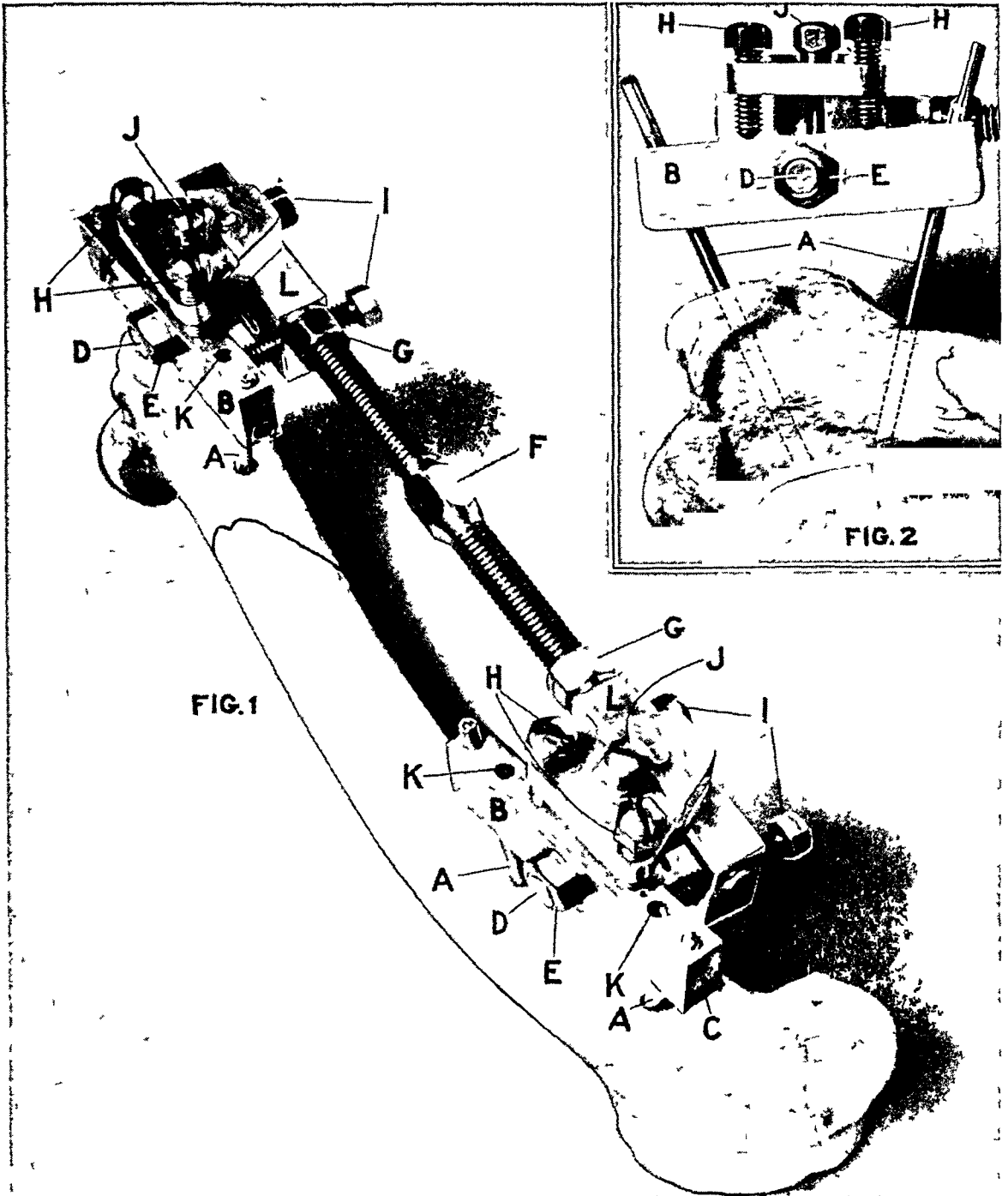


PLATE I—Fig. 1 and insert (Fig. 2) These are fully described in the relevant text

seat well into the distal cortex and when the pin is inserted it should be forced through the opposite cortex by pressure and rotation.

An alternate method is to insert the pin into a Magnuson motor-driven drill handle, adapted to receive the pin. No preliminary drilling is required, but care must be taken to see that the pin is not driven too far through the distal cortex.

If, in the first roentgenograms taken after the instrument has been applied, it is found that the pins project through the distal cortex too far into the soft parts, they can be withdrawn to the proper depth.

As soon as the first pin has been inserted the handle is unlocked from the pin and another pin fitted into the handle. The second pin is then introduced through the proper pin hole in the same pin bar while an assistant raises the pin bar about one-quarter of an inch above the surface of the skin. The second pin is then applied in a similar manner as the first, emerging through the inner cortex as above described.

The second pin assembly is then placed in position. When all four pins have been placed, they should be locked with the small hexagonal wrench by means of set screws in the end of each pin bar.

Applying the Extension Bar—Adjusting screws I and H should be unscrewed so they will not interfere with slipping the extension bar on to the pin bars. Lock nuts G on extension bar should be loosened so as to facilitate extension or contraction as well as rotation. From a strictly mechanical point of view there is no reason why, if one had two inches of overriding in a given fracture, the extension bar could not be so adjusted that it would slip onto the pin bars with this degree of overriding being present, with the idea of then proceeding to overcome shortening and then the other types of displacements. From experience, however, it has been shown that much time can be saved if the operator will grasp the pin assembly in each hand and manually overcome as much of the overriding as possible, before applying the lateral extension bar. In this way fully 75 per cent of the reduction maneuvers will be accomplished in 30 seconds time. While the operator maintains this position (Fig 3) the assistant adjusts the extension bar to the right length and slips the stud bolts (D) through the holes in the pin bar and then proceeds to screw on the nut (E). Before the operator lets go of the pin bar assemblies, the adjusting screws I and H are snugly set with the fingers only.

Extension—By properly manipulating extension bar nut (F) the proper degree of extension can be easily secured. This can be checked in many instances by deep palpation.

Mediolateral Alignment—A mediolateral alignment of either segment is secured by proper manipulation of adjusting screws H. Obviously, when this adjustment is being made, nut E should be slightly loosened. After it has been secured, nut E should be firmly tightened.

Anteroposterior Alignment—Each segment can be manipulated in this plane by set screws I. The patient is then moved to the Radiologic De-

partment, where final manipulations are accomplished either under fluoroscopic guidance or by taking several roentgenograms

The question has often been asked as to whether the pins should be put in place with the aid of the fluoroscope? The answer is definitely "No"

- 1 Too much fluoroscopy would be necessary, which would endanger the patient and the operator
- 2 By having an accurate knowledge of the anatomy involved, fluoroscopic guidance is unnecessary



FIG 3 —Showing pins and pin bars in place, and extension bar about to be applied

- 3 Sterile surgery is impractical in the Radiologic Department

A very important factor in the treatment of fractures is to see that firm impaction of the fragment is secured. As a final adjustment it is well to slightly impinge the fragmented ends upon each other.

By firmly setting all adjusting screws, the entire instrument becomes locked and now acts as a splint.

CASE REPORTS

Four typical cases are reported in some detail. These were selected at random but illustrate some of the advantages of the Stader splint.

Case 1 —N W, age 22, was admitted to Bellevue Hospital, March 16, 1941, with an oblique fracture of the right tibia and fibula. A plaster encasement was applied, March 16, 1941, and the postreduction film showed excellent position. He was discharged, March 19, 1941, with crutches, but without bearing weight. On April 2, 1941, he returned complaining of severe pain in the leg. Roentgenograms showed what usually happens to an oblique fracture of the tibia and fibula when put in a plaster encasement.

FIG 4

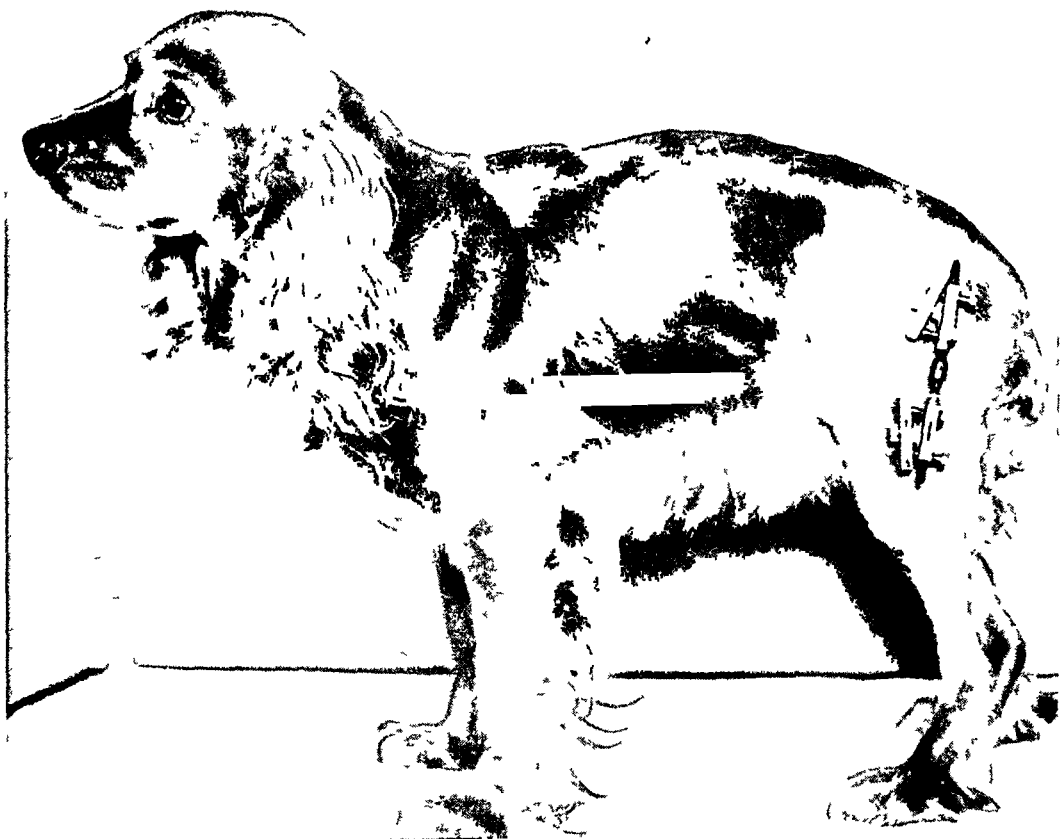


FIG 5

FIG 4—Showing a dog with a fracture of the femur—Stader splint in place
FIG 5—A and B Splint in place C Splint removed—pin holes healing

STADER REDUCTION SPLINT

before union occurs. Overriding and some angulation had developed and a good weight-bearing leg was improbable. On April 2, 1941, the encasement was removed and a Stader splint applied. The position of the fragments was excellent and walking was started within a few days. On April 11, 1941, he returned to work and continued working with no loss of function of his leg and no complaints. There was no seepage from any of the pins. On June 9, 1941, he had firm and solid union roentgenologically.

FIG 6



FIG 7

FIG 6—Case 1. Fracture of Tibia and Fibula. A. Malposition in plaster. B. Apparatus in place—fracture reduced. C. Showing union—apparatus removed.

FIG 7—Case 2. Fracture of Shaft of Humerus. A. Before reduction. B. Apparatus in place but fracture not completely reduced. C. Reduction completed after return to the ward.

The splint was removed. No further treatment was necessary. Three days later the dressings on the pin holes were removed and complete healing occurred within a week. This was an ideal case in that, with complete cooperation, he lost no time from his work and union occurred in an exceptionally short period of time (Fig 6).

This case demonstrates several points:

- (1) An oblique fracture cannot be adequately immobilized in a plaster encasement. In our experience, slipping of the fragments frequently occurs.
- (2) The fracture, in spite of being two weeks old, could still be reduced with the Stader apparatus.
- (3) Union occurred rapidly, with the firm immobilization that this apparatus afforded.

Case 2—G G, male, colored, age 47, was admitted to Bellevue Hospital, December 26, 1937. He had sustained a fracture of the left humerus shortly before admission, with musculospiral nerve paralysis. A Stader apparatus was applied, and excellent reduction obtained. The splint was removed, March 5, 1938, and the arm placed in a sling. The pin holes healed promptly, and he was discharged, March 16, 1938, with a cock-up splint to correct a wrist drop. On March 21, 1938, examination showed firm union at the site of fracture and the pin holes healed. The wrist drop was treated with cock-up splint and galvanic current therapy. On June 20, 1938, the musculospiral paralysis had almost entirely cleared. He had full function of the elbow and shoulder joint, and has remained well and returned to work, with no symptoms (Fig 7).

This case shows the usefulness of the Stader apparatus in fractures of the shaft of the humerus.

Case 3—A D, white, male, age 36, was admitted to Bellevue Hospital, August 30, 1941. He had been hit by an automobile just before admission, and sustained a badly comminuted compound fracture at the junction of the lower and middle thirds of the tibia and fibula. The wound was adequately debrided, under general anesthesia, and a Kirschner wire was inserted through the os calcis and skeletal traction was applied. On September 2, 1941, a posterior molded plaster splint was applied while in traction, and the traction maintained. Three weeks later a circular plaster encasement was applied over the posterior molded splint, after packing the compound wound with vaselined gauze. The traction was discontinued. Roentgenograms showed good alignment and the patient was discharged walking on crutches. He was readmitted to the hospital on three occasions for change of encasement due to the profuse discharge and odor. The wound was freshly packed with vaseline gauze at each admission. The roentgenograms showed the same good position but never any evidence of callus formation nor any evidence of wound healing. At the end of seven months, in March, 1942, roentgenograms showed no callus, and the wound was draining a large amount of pus. It was felt that the lack of healing was probably due to the fact that the plaster encasement did not give a sufficient and adequate immobilization. In an effort to obtain more rigid immobilization a Stader splint was applied. Active motion was started in the knee and ankle joints, as these joints were badly stiffened due to the long period of plaster immobilization. He was discharged from the hospital with a dressing on the compound wound, bearing some weight and being treated with occupational therapy for joint mobilization. The joint function has improved 75 per cent. The compound wound showed rapid, progressive healing after the splint was applied. The discharge from the wound diminished rapidly and the dressing needed to be changed only every two weeks. The denuded bone covered rapidly with granulation tissue. Roentgenograms, on May 1, 1942, showed a fair amount of callus formation.

It was with great hesitancy that the Stader apparatus was applied in this case because of the infection present at the fracture site. The firm immobilization which the Stader splint produced allowed the infection to subside, reduced hyperemia, and helped callus formation. The seven months of immobilization in plaster caused severe stiffness of the knee and ankle joints and atrophy of the muscles. Mobilization of these joints was possible after the application of the splint. Muscle atrophy was corrected by weight-bearing and active motion at the knee and ankle joints.

Case 4—A B, male, age 52, was admitted to the hospital October 26, 1940. Two hours before admission, he had sustained a fracture of the lower third of the left tibia and fibula. A plaster encasement was applied but the position of the frag-

STADER REDUCTION SPLINT

ments was unsatisfactory. A Stader splint was then applied. Due to the small lower fragment, it was impossible to apply two pins in the usual fashion. The splint was then modified to fit this problem by changing the shape of the pin bar so that one pin could be inserted in the lower fragment in an anteroposterior direction and the second pin in the lower fragment could be applied in the usual manner. A curved pin bar was made to fit over these pins. The pins in the upper fragment were applied



FIG 8—Case 4. Fracture of Tibia and Fibula, with a Short Lower Tibial Fragment
A. Before reduction
B and C. Reduction with Stader splint
D and E. Showing union, with apparatus removed

in the usual manner and the standard extension bar fitted to the two pin bars. Adjustments were made and good anatomic alignment secured. The patient walked early, but the apparatus had to be left in place for 210 days before solid union occurred. No further treatment was necessary as the knee and ankle joint had normal range of motion and the pin holes healed in six days (Fig 8).

The solution of reduction and splinting of fractures very low in the shaft of the tibia and fibula could not be accomplished with the original apparatus

as the bone space which the two lower pins would have to occupy was too short. The apparatus was then modified to be able to apply this method to the very low fractures with short lower fragments.

TABLE I
STATISTICAL DATA OF 20 CASES TREATED WITH THE STADER SPLINT

Name	Sex	Age	Fracture	Apparatus in Place	Days before Union	Seepage	Infection	Complications	End Result*
E S	M	53	Tibia & fibula	9/20/38-12/6/38	77	Slight 4 pins	None	None	4-4-4
W W	M	43	Tibia & fibula	10/29/37-1/27/38	91	Slight 2 pins	None	None	4-4-4
J M	M	53	Tibia & fibula	2/2/38-6/5/38	124	None	None	None	4-4-4
M S	F	52	Tibia & fibula	10/25/38-2/23/39	122	Upper pin	None	None	4-4-4
L H (Fig 9)	M	53	Tibia & fibula	11/8/38-1/23/39	76	None	None	None	4-4-4
J L (Fig 10)	M	56	Tibia & fibula (compound)	11/2/38-3/27/39	145	None	None	None	4-4-4
G G	M	47	Humerus	12/26/37-3/5/38	69	None	None	Musculospiral paralysis	4-4-4
A B	M	52	Tibia & fibula	10/30/40-6/11/41	320	None	None	None	4-4-4
H S	M	43	Tibia & fibula	12/21/41-4/1/42	102	Upper pin	None	Intertrochanteric fracture pubic fracture alcoholic psychosis	4-4-4
J H	M	43	Tibia & fibula	4/6/41-6/29/41	84	Lower pin	Abscess about lower pin	None	4-4-4
F G	M	28	Tibia & fibula	4/2/40-7/10/40	99	None	None	None	4-4-4
J B	F	38	Tibia & fibula	4/6/40-6/24/40	80	None	None	None	4-4-4
J B	M	70	Tibia & fibula (compound)	2/21/42-present		Three upper pins	None	Diabetes	
A D	M	36	Tibia & fibula (compound)	3/24/42-present		Upper pins	None	Compound fracture	
N W	M	22	Tibia & fibula	4/2/41-6/9/41	68	None	None	None	4-4-4
M M	F	34	Tibia & fibula	10/30/41-1/3/42	65	None	None	Syphilis	4-4-4
J C	M	48	Tibia & fibula	2/7/42-4/23/42	76	Lower pin	Abscess	Abscess app removed 4/23/42	4-4-4
R K	M	36	Tibia & fibula	11/29/37-3/31/38	123	Lower pins	None	Frac malleoli tibia and fibula frac skull	4-4-4
C G	M	81	Femur shaft	11/14/37-12/22/37		Upper pins	Abscess about upper pin Osteomyelitis	Osteomyelitis Death	Death
M J	M	54	Tibia & fibula (compound)	4/26/40-6/30/40	65	None	None	None	4-4-4

* The end-results have been estimated according to the Massachusetts General Hospital classification. This estimation is made on an anatomic, economic and functional basis: 1 = 25% of normal, 2 = 50% of normal, 3 = 75% of normal, and 4 = 100% of normal.

The headings in Table I are self-explanatory. The column marked seepage does not indicate infection. It means that at the junction that the pin made with the skin there was a small amount of serous discharge,



FIG 9—Case L H Fracture of Upper Third of Tibia and Fibula
A and B Before reduction
C After reduction with Stader splint Note that the pins in the upper fragment protrude through the distal cortex farther than is to be desired These pins should have been withdrawn somewhat before they were locked in the pin bar



FIG 10—Case J L Compound Fracture of Middle Third of Tibia and Fibula
A Encasement in plaster, showing malposition
B Encasement removed—reduction with Stader splint
C Showing union—splint removed

which usually formed a crust about the pin When the pin was removed healing occurred within a few weeks Since the pin bar has been made of a plastic instead of metal the seepage has decreased so that there are 10 cases in which no seepage took place

This seepage is due to galvanic current set up by the use of two different metals, the pin being stainless steel and the pin bar duralumin The electrical potential as measured by a galvanometer with the two different metals was as follows

Between the 1st and 2nd pins	35 units
Between the 1st and 3rd pins	25 "
Between the 1st and 4th pins	4 "
Between the bar and 1st pin	15 "

Between the bar and 2nd pin	1 5	"
Between the bar and 3rd pin	1 5	"
Between the bar and 4th pin	1 5	"

The same readings made with the plastic material for pin bars were

Between the 1st and 2nd pins	0 5	units
Between the 1st and 3rd pins	0 2	"
Between the 1st and 4th pins	0 2	"
Between the bar and 1st pin	0	"
Between the bar and 2nd pin	0	"
Between the bar and 3rd pin	0	"
Between the bar and 4th pin	0	"

In other words the metal-to-metal contact gives a high dielectric value, whereas with a material of high insulating value the electrical potential is *nil*

There were three real infections, in two of which abscesses formed and had to be incised and drained. They healed quickly after incision, without any evidence of osteomyelitis. One infection, the femur case, resulted in severe infection with osteomyelitis and death. In this patient, an old man, age 84, the dressings and the pins were continuously contaminated with urine and feces, due to involuntary micturition and defecation. The patient was constantly picking at and removing the dressings, so that it was impossible to avoid secondary contamination of the pin wounds.

CONCLUSIONS

(1) A new splint for reducing and immobilizing fractures of the shafts of the long bones is presented.

(2) Early transportation of the patient is possible, as contrasted to the impossibility of early transportation where traction suspension is used. This is of importance in bombed areas, either in civil or military surgery.

(3) The splint is simple to apply, and correction of malposition of the fragments is possible in all three planes of space even up to the time that fibrous union has occurred.

(4) Early weight-bearing and continued use of the contiguous joints is permitted and urged and this prevents muscle atrophy and stiffening of the joints from occurring.

(5) After-treatment is reduced to a minimum as muscle strength is retained and joint function carried on.

(6) Seepage around the pins is usually due to galvanism and not to infection. It is not an indication for removing the pins unless accompanying signs of inflammation are present.

REFERENCES

- ¹ Schanz, A. *Munchen med Wchnschr*, 69, No 25, 930-931, June 23, 1922.
- ² Riedel, G. *Zentralbl f Chir*, 57, No 2, 84-86, January 11, 1930.
- ³ Schanz, A. *Arch f klin Chir*, 69, 494-517, 1932.
- ⁴ Stader, O. *North Am Vet*, 18, No 1, p 52.
- ⁵ *Idcm* *North Am Vet*, 20, No 1, p 55.
- ⁶ *Idcm* *North Am Vet*, 20, No 2, p 54.
- ⁷ *Idcm* *North Am Vet*, 20, No 3, p 62.
- ⁸ Parkhill, C. *Trans Amer Surg Asso*, 15, 251, 1897.
- ⁹ Freeman, L. *ANNALS OF SURGERY*, 70, 231, 1919.

BRIEF COMMUNICATION



A NEW RECTOSIGMOIDAL BIOPSY FORCEPS

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NEW YORK, N Y

THE INSTRUMENT, illustrated in Figure 1, is designed primarily for obtaining rectal and sigmoidal biopsy specimens. This biopsy specimen forceps embodies several new features. The shaft with the cutting jaws at its distal end has a rotating mechanism with a locking device near the handle, permitting 360 degrees rotation of the jaws. Thus, the shaft of the forceps can be rotated so that the cutting jaws will face directly a suspected lesion located anywhere in the circumference of the rectum or sigmoid (Fig 2). Furthermore, the cutting jaw mechanism operates at an angle of about 30 degrees from the axis of the shaft and consists of a stationary and a

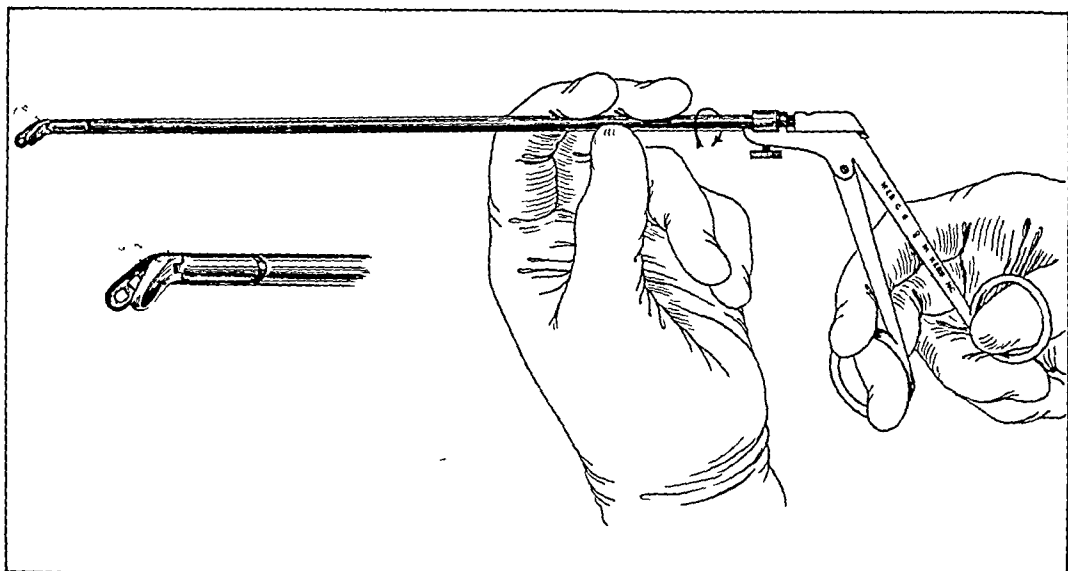


FIG 1—Showing the biopsy forceps and a diagrammatic view of the rotary movement of the shaft

moving jaw, the latter opening and closing sidewise (Fig 2A). The sidewise operation of the moving jaw makes for better visualization of the tissue engaged in the cutting jaws until they are closed (Fig 3), this is especially true in the case of the small polypoid lesions. Thus, with this biopsy specimen forceps, mucosal excrescences and small sessile or pedunculated adenomata can be removed for microscopic study with ease and safety prior to fulguration*.

* I have emphasized the clinical importance of these lesions in a recent review of the literature (*Am J M Sc*, 202, 282, August, 1941) by showing that many authorities regard mucosal excrescences and polypi of the rectum and sigmoid as precursors of frank malignancies in certain cases.

The biopsy forceps herein described is equipped with scissors handles to apply positive pressure for opening and closing the jaws. The moving jaw fits inside the cutting edge of the stationary one, thus assuring a clean-cut specimen by the shearing action of the jaws, no overhanging lips interfere with the clean excision of tissue. The jaw capacity is ample, the stationary

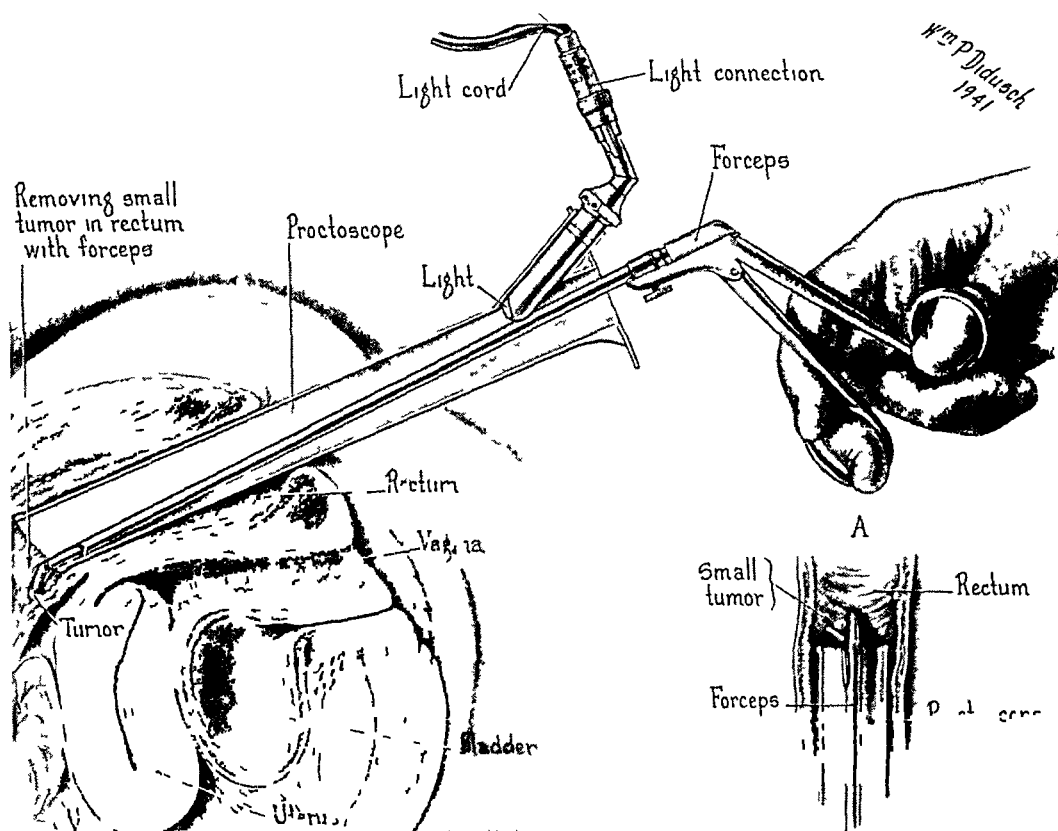


FIG. 2.—Sagittal section showing the removal of a small sessile polyp with forceps (A) Showing angle of jaws of forceps as viewed from above

jaw has two openings to prevent the crushing and distortion of the specimen. At the same time the bars formed between those openings prevent the loss of the excised specimen. The instrument is sturdily built and is manufactured in different working lengths, the one illustrated here is 40 cm. long.

My thanks are due to Mr. F. C. Wappler and Mr. H. S. Rubens, of the American Cystoscope Makers, Inc., New York, N. Y., for their technical advice, and to Mr. W. P. Didusch for the illustrations.

RECTOSIGMOIDAL BIOPSY FORCEPS

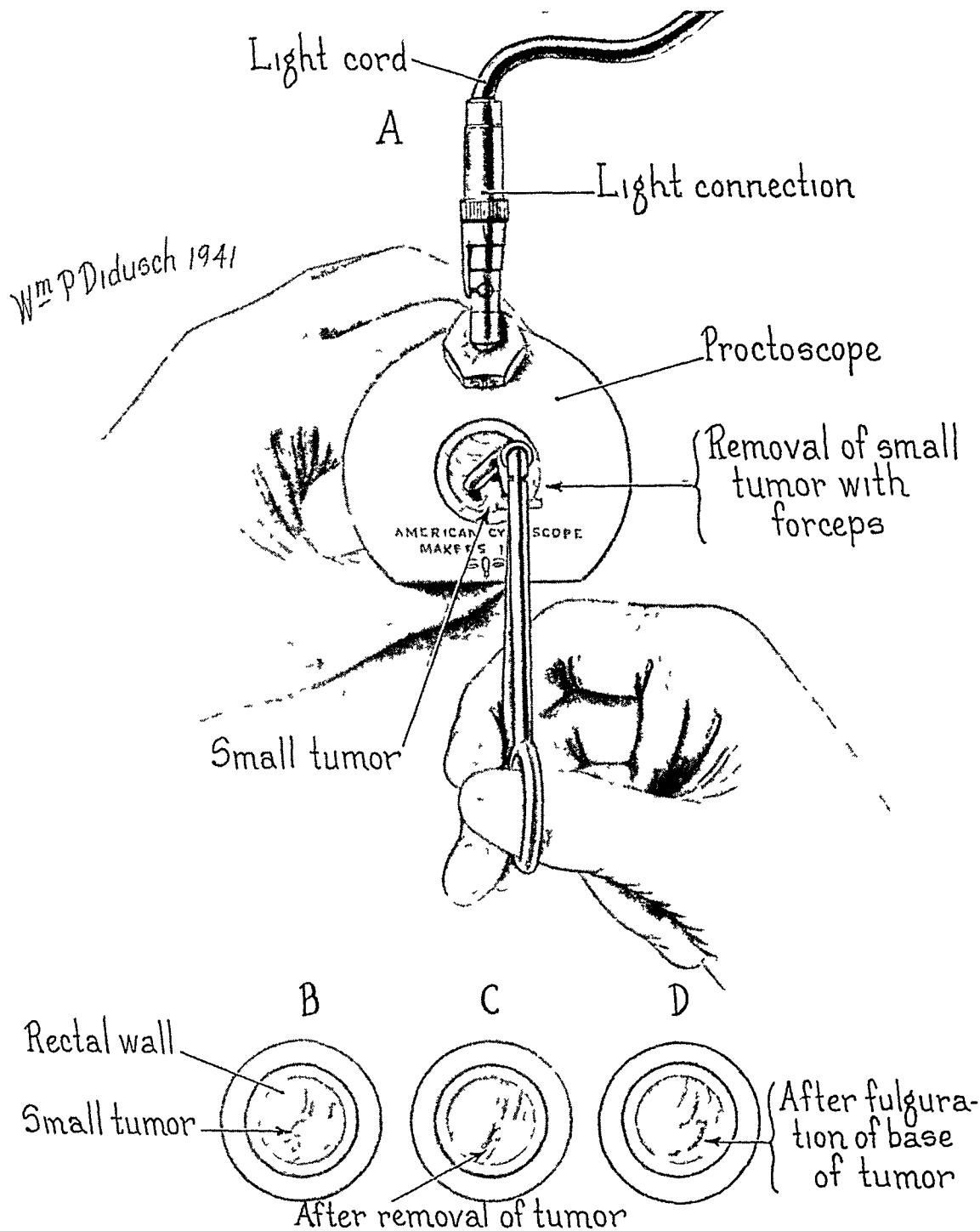


FIG 3—(A) Actual view of tumor in relation to the jaws of forceps (B) View of tumor *in situ* (C) Appearance of base of tumor after removal (D) Appearance of base of tumor after coagulation

BOOK REVIEW

INTESTINAL OBSTRUCTIONS (Second Edition) BY OWEN H WANGENSTEEN, M D

Published by Charles C Thomas—1942

A second edition of Wangensteen's monograph on Intestinal Obstruction is timely because of certain contributions, such as those of Miller and Abbott, which have been made to the subject since the publication, in 1932, of the manuscript for which he was awarded the Gross Prize

That all of these reports in literature have served to confirm and develop Wangensteen's thesis of intestinal decompression is indeed remarkable, but in this second edition, and in the same masterly way as in the first, he presents all the phases of the problem—etiology, mechanism, and treatment

In the discussion of the treatment he can now better evaluate the indications for and the dangers of intestinal decompression by tubes, because of his experience and that of others during the intervening ten years. His statement, that it must be realized both by the internist and surgeon, that there is a limit to the use of conservative decompression beyond which it is unjustifiable to delay surgical intervention, must be accepted as authoritative

To make such a vital decision requires complete collaboration on the part of the internist and the surgeon, and Wangensteen makes this perfectly clear in this "new testament" of his original essay, which is without question essential as a supplement to the first edition, and also as a summary of our present knowledge of the problem of intestinal obstruction

WALTER ESTELL LEE, M D

EDITORIAL ADDRESS

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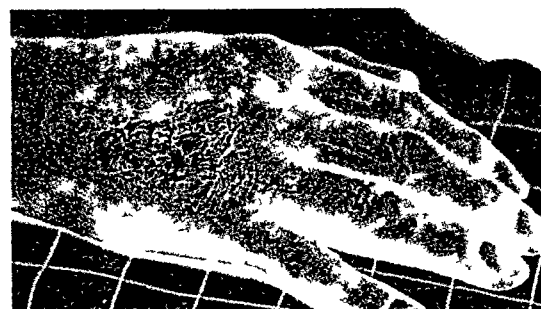
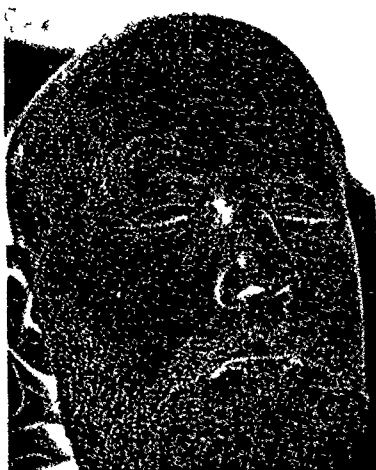
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Colored photographs of a burn treated by the author's technique

The top picture shows a three day infected superficial burn of the face and slightly deeper burn of the dorsum of the hand and wrist. This picture was taken on the day following night admission the burn having been cleaned and dressed during the night. The dressing was removed for the picture. Below it are pictures of the face on the 4th and 12th day after admission when healing was complete, and pictures of the hand on the 4th 8th and 12th days, when epithelization was complete and only a protective cotton gauze was needed



A PRACTICAL CONCEPT FOR THE TREATMENT OF MAJOR AND MINOR BURNS

THE IMPORTANCE OF TIMING THEREIN

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THE MANAGEMENT OF THE VICTIM of severe burns has always presented one of the major problems of surgical experience. During, and since the first phase of the World War I, 1914-1918, many surgeons and investigators devoted much time and effort to a study of the principles and details of such management. These investigations have had for their aim the preservation of life and return to useful citizenship of the victims of such misfortunes with as little loss of time as possible. That the attainment of either of these desiderata is not easy or certain is attested to by the fact that there is still no unanimity of opinion as to the best method of local treatment.

The present conflict has hitherto been characterized by an enormous increase in burned persons. These cases have been the result of an aerial bombardment of civilians, fire in the cockpit or fuselage of aircraft, oil and flash burns on shipboard, both mercantile and naval, and as the result of the general employment by all combatants of tanks. It is probable, moreover, that in the very near future flame throwers and the employment of corrosive gases will present further problems.

In an attempt to elucidate the problems indicated above, there have appeared, more especially since the present phase of the war began, many publications by proponents and protagonists of several essentially different techniques—some new and some previously proven methods. Among these different methods the more important are probably tannic acid with or without silver nitrate as an adjuvant, triple dye jelly or solution, normal sodium chloride solution and/or hypochlorite employed as bath, compress or bag (Bunyan)¹³. Needless to say, the introduction of sulfonamides has been tested by numerous surgeons and experimental workers. It would appear that in the hands of those thoroughly trained in the individual techniques each of these methods may be used with profit.

It is not our intention in this communication to add to the confusion which to a certain extent envelops the subject. It is our purpose, however, in a

modest fashion, to outline a method which, in our hands, has proven itself to be satisfactory, simple and safe. This definite plan of treatment is comprehensive enough to include the use of any well recognized and accepted therapeutic principle.

We wish, at the outset, to emphasize the necessity for having such a plan for the treatment of major burns, whether in the armed services, or in civil industrial practice, especially in the emergent situation of today. The plan we have adopted at the Montreal General Hospital is based on "timing" as understood in all modern treatment. This is not a new principle. Perhaps it has hardly been emphasized enough in scientific medical teaching. We submit that, for the successful practice of surgery today, constant practical application of accurate timing in treatment is essential. It is as necessary in the medical world as in all phases of modern life whether in war or peace. Our plan is outlined in some detail in the accompanying illustrations, charts, and tables. It has been employed successfully at the hospital for several months.

The history of modern burn treatment may be roughly divided into four consecutive periods, each merging into the other, each marking an advance in knowledge, all resulting in progressive and continuous improvement in mortality percentage, and in local functional and aesthetic results. These deductions are well shown in the statistics from leading clinics. The periods referred to are

- (1) That previous to the adoption of tannic eschar treatment
- (2) The period marked by the adoption of the principle of tannic eschar treatment as suggested by Davidson (1925)¹⁶
- (3) The period following this, marked by full recognition of the rôle of shock,^{8, 9, 14, 15, 20, 21, 27, 28, 34, 35} and the gradual development of means to combat it, in particular the controlled use of blood substitutes. This period actually began much earlier but has only been generally recognized during the last decade.
- (4) The period subsequent to the introduction of sulfonamide therapy for topical application—about 1940.

The improvement during these periods was well shown by Farmer,¹⁸ in a recent paper read before the American Association of Surgery of Trauma in Boston, with percentages of 35–16–11 and 2.5 per cent for the corresponding periods at the Sick Children's Hospital, Toronto, Canada. The improvement in morbidity and functional results is just as striking. On this side of the problem certain details of local treatment have played important rôles, i.e., the importance of early skin grafting, and the abandonment of restrictive eschar treatment on hands, fingers, etc.

When and where the above facts are fully realized, the surgeon will see that any attempt to substitute or revise any phase of burn treatment must take full cognizance of these factors. In full recognition of this, we have planned our treatment to include the basic principles above mentioned, and timed the plan to *anticipate* each of the problems commonly met with in turn, namely (1) Shock, during the first 24–48 hours, (2) Toxemia, from the second to

the fifth day (3) Sepsis during the subsequent week or 10 days (4) Finally, scarring and contractures (See Table III for details)

At this point, it is necessary to refer to several features of the burn problem which have such direct bearing on results that they may influence the surgeons' treatment

- (1) The extent of surface area of the burn—In this connection, the recent tendency to divide the burns into *major* and *minor* problems, as encouraged in Britain particularly, has helped to simplify matters (Berkow's Tables⁶ are used in our surface estimations)
- (2) Important as the foregoing is, it must be modified or qualified, at once, by reference to the agent responsible for the burn, such as actual fire, hot liquid, electricity, chemicals, radiant heat, hot metals, etc. In this connection the length of exposure to the burning agent must also be considered. These comments require no elaboration to the initiated
- (3) The well known comparative severity of burns in children
- (4) The elapsed time between the burn and treatment. In major burns this may be extremely important as regards shock, and 30 minutes may be said to be a long time under the best conditions. Minor burns, on the other hand, frequently are neglected for several days, when infection and its consequences may change them into more serious problems
- (5) Other factors contributing to shock, such as exposure to the elements, fatigue, exhaustion, lack of food and water, etc., particularly in the fighting services
- (6) Concomitant injuries may be severe and greatly complicate treatment. Burns in the air force or air accident crashes frequently present very serious and even fatal injuries of other kinds
- (7) The type and extent of first-aid care, particularly as regards exclusion of air and maintenance of body warmth
- (8) Finally, with regard to the depth of the burn and the various classifications used to describe this. The writers believe that the only decision needed is whether skin-grafting will be necessary or not. Therefore, as it is difficult, if not impossible to gauge the depth accurately in the early stages, the arguments regarding different classifications seem superfluous. Wakeley³¹ has pointed out that five days is the minimum for recognition of depth

PROCEDURE IN MAJOR BURNS OF THERMAL TYPE

Having regard for the above facts and previously mentioned sequence of complications to be anticipated, the timed schedule of treatment is carried out as in Table III. To do this most effectively requires careful prearranged organization of personnel, equipment, and supplies

Regarding personnel, it has been found best to have separate burn and shock teams, each composed of one attending surgeon, one resident and interns,



FIG 2

FIG 1—Showing burn tent opened
FIG 2—Showing burn tent closed

all operating under a senior surgeon. Trained graduate nurses and orderlies are also part of our set-up. Equipment includes special burn tents shown in Figures 1 and 2. Supplies should include an adequate amount of stored plasma or serum, tannic acid, silver nitrate, 5 per cent sulfathiazole emulsion and 4" x 6" cuts of 1 or 2 Mm curtain-mesh.

On admission, the major burns are placed at once in the burn tent, and the temperature gradually, not rapidly, raised to 80° F. The shock team functions first, estimating the hemoconcentration, and immediately administering plasma diluted 50 per cent by saline. This is done by a continuous drip in a cut-down intravenous, *via* the long saphenous vein at the ankle. A cannula, and not a needle, is used as a routine. It may be necessary to milk the plasma into the vein at the start. We have evolved a special double roller for this purpose.

When the above measures have been instituted, usually about one hour after admission, local treatment is begun. Operating room technique is used in the ward, in the tent bed, and only very rarely is anesthesia employed. Morphine gr 1/4 is administered on admission and repeated during the first hour if necessary (synergistic effect). For large surface areas (trunk or thigh), when life-saving is involved, tannic acid-silver nitrate eschar^{7, 16} is used. So far, we have not found a better type of eschar. In all critical areas, in moderate areas otherwise, and for all minor burns, we are using a thick pressure-type dressing^{2, 3, 4, 24}. A mask is used for the face. We have modified the dressing by using a basic dressing of 5 per cent sulfathiazole oil in water emulsion (M G H formula), as described in detail by one of us (Ackman)^{1, 2} in 1942, and has been found to be a highly successful method of preventing infection, or controlling it in delayed, contaminated, or actually infected cases. The details of the development and preparation of the emulsion, as well as our experience with it in burn therapy, and other surgical practice, have been described in the literature this year^{1, 2}.

The topical use of sulfonamides in crystalline form, in powder, paste, suspension or emulsion, is already well established, so much so that to eliminate this form of treatment in burns would be a backward step. Before applying an eschar it is possible to powder a burned surface, and similar treatment may be used at other times. In critical areas, for all practical purposes, we have found the M G H emulsion offers a particularly satisfactory adjunct to pressure dressings. The bacteriostatic action prevents or controls infection and, because of this, the frequency of the redressing may be timed. It is usually possible to leave the original dressing or for at least one week without discomfort and with little odor, more often none. Moreover, this emulsion dressing affords a single continuous form of treatment from first-aid to final healing, even with grafting.

Local tissue concentrations of sulfathiazole are surprisingly high, 120 mg + per cent in 24 hours, blood levels are low and fleeting (maximum 3.5 in one hour) even with large amounts (10 ounces) of the emulsion. We recognize as have others, the anesthetic action of the sulfonamide, akin to the effect of benzocaine.

It is interesting to note that when primary debridement is complete the emulsion dressings may be left in place for as long as two weeks without disadvantage. On the other hand, should the burned area require some revision or inspection during the first few days, as when progressive skin separation occurs, redressing is comparatively painless and free from bleeding. The use of the basic "sulfamesh" is an important factor, which permits inspection of the burned area at any time, and it need not be changed. The sulfathiazole emulsion dressing, with its strong bacteriostatic action, materially assists early healing of superficial burns (6-7 days). In deeper burns, it permits early skin grafting and thus hastens the timing schedule.

We find the use of the emulsion facilitates the softening and separation of slough in severe cases. It is not necessary in these cases to completely replace and renew the basic "sulfamesh" dressing. Generally speaking we find it quite sufficient to supply additional emulsion on the renewed gauze layer.

The M G H emulsion, we believe, has distinct advantages over any other medium hitherto presented. It is simple and clean to handle. It offers economy in nursing and medical attention, and in the materials required. Its constituents are readily available and inexpensive. Sterility tests are negative, while its stability at extremes of temperature has been proven. The anesthetic effect is noteworthy.

EMULSION SULFATHIAZOLE 5% (M G H FORMULA)

Sulfathiazole (finely powdered)	5%
Triethanolamine	2%
Distilled water	24%
White beeswax	5%
Liquid paraffin	64%

TECHNIQUE

Step-by-Step Procedure

1. Treat shock first (See Table III for details)
2. With aseptic technique, cleanse burned area with soapsuds made from castille soap—without anesthesia
3. Wash with saline
4. Apply single layer of 4" x 6" "sulfamesh" strips* (1-2 Mm mesh), prepared beforehand or at time of treatment. Individualize fingers, *etc* (This basic dressing may be left on at redressings). Mask is used for the face.
5. Apply over this ordinary gauze dressings of 3-4 thicknesses, generously impregnated with emulsion. Do not individualize fingers, *etc* (Fig 3)
6. Pressure dressing, with cotton waste outside this. Do not individualize fingers, *etc*
7. Wrap in sterile towel or towels
8. Bandage firmly, with 4"-6" flannel or flannelette bandages cut on the bias,† or dressing gauze roller bandages 4-6 layers in thickness, or ordinary roller bandage if the former are not available (Fig 4)

* Cut from curtain material of 1 or 2 Mm mesh. In Canada called English curtain-mesh. May be obtained from T. Eaton Co. Ltd.

† Suggested by Dr. J. Carl Sutton of our surgical staff.

9 A plaster moulded splint is added for hand, forearm, *etc* in the functional position (Fig 5)

Steps 6, 7, 8 and 9 minimize contamination Note In redressing, at whatever date, the "sulfamesh" is not changed unless débridement is indicated This technique reduces pain and bleeding to a minimum, and permits removal of outer dressings to be performed more easily

FIG 3



FIG 4

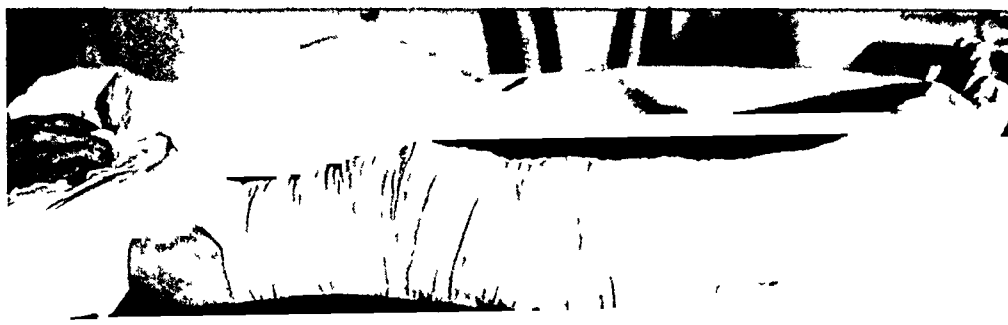
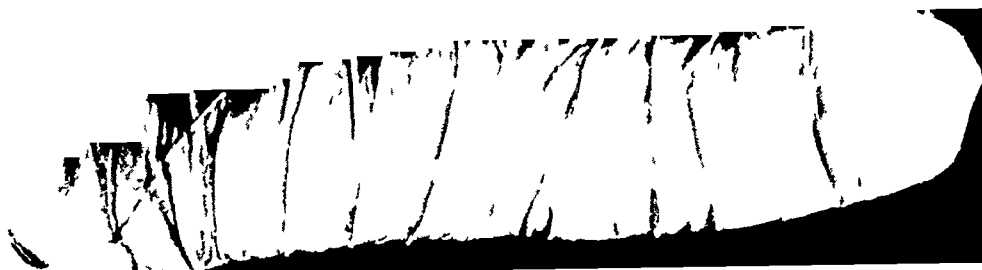


FIG 5

FIG 3—Showing basic "sulfamesh" dressing

FIG 4—Showing completed burn dressing

FIG 5—Showing completed burn dressing with posterior plaster mould

TABLE I
SUMMARY OF DATA OF 120 CASES OF BURNS TREATED

Number of major burn cases	31
Number of minor burn cases	89
Total number of burn cases	120
Thirty-one major burns as above—2nd°* only	19
Mixed 2nd° and 3rd°	12
Healing time of 2nd° burns	Longest 18 days Shortest 6 days Average 7—10 days
Healing time of 3rd° burns	Longest 66 days Shortest 21 days
(Including skin grafting)	15
Number of skin grafts (split grafts)	
(100% 'take' in all cases)	

INFECTIONS

General sepsis after treatment	None
Local sepsis after treatment	None
Pretreatment infections resulting from delayed admission—15 All controlled by first dressing (One only <i>Staph pyogenes hemolyticus</i> with some difficulty Sulfathiazole-resistant type) ³⁷	

COMPLICATIONS

Deaths	None
Number of sulfonamide rashes	Two
(Corrected by switch to 10% sulfanilamide emulsion)	
Number of toxic fevers	None

* Classification used—three degrees only

TABLE II
LABORATORY INVESTIGATIONS SHOWING THE CONCENTRATION OF SULFATHIAZOLE
IN LOCAL TISSUES TREATED WITH THE M G H EMULSION*Dressings not Changed*Elapsed Time after Treatment—Average of Estimations in Mg Per Cent
(Total Sulfathiazole Only)

Clinical Cases	M G H Laboratory	Independent Laboratory*
24 hours	120 mg per cent	124 mg per cent
48 hours	78 mg per cent	76 mg per cent
72 hours	45 mg per cent	43 mg per cent
4 days	34 mg per cent	—
5 days	30 mg per cent	—
7 days	28 mg per cent	—
Laboratory Animals	M G H Laboratory	Independent Laboratory*
24 hours	122 mg per cent	129 mg per cent
48 hours	—	65 mg per cent

BLOOD LEVELS OF SULFATHIAZOLE IN LOCAL TISSUES TREATED WITH THE M G H EMULSION
Dressings not Changed

Clinical Cases	M G H Laboratory	Independent Laboratory*
1 hour	Total 3.5 mg per cent	—
2 hours	3.1 mg per cent	—
3 hours	3.0 mg per cent	—
12 hours	1.3 mg per cent	—
24 hours	None to trace only	—
Laboratory Animals	M G H Laboratory	Independent Laboratory*
1 hour	—	12.1 mg per cent
2 hours	—	7.6 mg per cent
3 hours	—	3.5 mg per cent total
4 hours	—	1.5 mg per cent
5 hours	—	Trace only
6 hours	—	None

* These independent laboratory experiments were maintained through the courtesy, cooperation and material assistance of Messrs Charles E Frosst & Company, Montreal Canada

TABLE III

TIMING IN THE HOSPITAL TREATMENT
THE MONTREAL GENERAL H

		PERIOD OF SHOCK 48 HOURS		
	FIRST HOUR	FIRST 24 HOURS	SECOND 21 HOURS	
GENERAL TREATMENT	HYPO <u>MORPHINE</u> $\frac{1}{4}$ GR REPEAT IN THE HOUR	CONTINUE <u>MORPHINE</u> AS MAY BE INDICATED DURING THIS PERIOD		SYPH
SHOCK TEAM 24-HR SERVICE		<u>CORTIN</u> 25 CC IN EXTREME CASES	CONTINUE CORTIN INTRA-MUSCULARLY 10 CC Q 6 H AS INDICATED FOR 3 OR 4 DAYS	NIM CATI SULI OUS URIN I GI
UNDER SUPERVISION SENIOR SURGEON		CONTINUE TO A MINIMUM OF 2,000 CC (PLASMA OR SERUM) FOR 10% BURN IN 48 HRS CONTINUOUS INTRAVENOUS DRIP CONTROL THE AMOUNT OF SALINE AND SERUM OR PLASMA BY HEMOGLOBIN READINGS		BIOO INFR GLUC BIOO
	HEAT — DEVELOP SLOWLY TO 80° UNDER TENT		ATS 1,500 UNITS	HI A OUT
	WATER BY MOUTH CONTAINING CARBOHYDRATE FOR FIRST 24 HOURS		<u>FLUIDS</u> AS TOLERATED	ILU I CC I
	<u>OXYGEN</u> ENDOPHARYNGEAL TUBE			DIT CARI
	<u>INTRAVENOUS</u> GLUCOSE SALINE IF NEEDED		ENEMA	LAL
LOCAL TREATMENT	<u>DELAYED</u> UNTIL INTRAVENOUS SHOCK TREATMENT BEGUN AND EFFEC-TIVE	<u>DÉBRIDEMENT</u> WITHOUT ANESTHETIC		UNRO APP LMU
BURN TEAM		<u>TRUNK, THIGHS, LEGS, FEET, ARMS, FOREARMS</u> SPRAY WITH 10% TANNIC ACID FOLLOWED BY 10% SILVER NITRATE REPEAT Q $\frac{1}{2}$ H UNTIL TANNED		
UNDER SUPERVISION OF SENIOR SURGEON		<u>CRITICAL AREAS</u> —SULFATHIA-ZOLE EMULSION DRESSINGS	DRESS AND DÉBRIDE ON 2ND DAY ONLY IF INDICATED	CRU DEI IND SLN
LABORATORY EXAMINATIONS	<u>HEMOGLOBIN</u> ESTIMATION OR <u>HEMATOCRIT</u> OR <u>R B C</u> COUNT	REPEAT Q 1 H UNTIL HEMO-CONCENTRATION CONTROLLED, AND THEREAFTER AT LEAST Q 4 H	<u>BLOOD CHEMISTRY</u> TOTAL PROTEIN (ALB AND GLOB) CHLORIDES SUGAR CO ₂ COMB POWER <u>CULTURES WITH DRFSINGS</u> <u>URINALYSIS</u>	BIO SUG UPF SUI BIO CUI UPI
CLINICAL DATA	<u>ADMISSION T P R</u>	<u>CHART</u> PULSE Q 1 H. B P Q 1 H HEMOGLOBIN % Q. 1 H — 4 HRS THEN Q 4 H TEMP Q 4 H INTAKE AND OUTPUT DAILY	T.P R Q 4 H. B P. AND P. CHART Q 1 H INTAKE AND OUTPUT DAILY	T.P P P CAT INT
CHART				

LABORATORY INVESTIGATIONS OF THE EMULSION

Molecular solubility of sulfathiazole in the emulsion, as checked in both M G H and an independent laboratory — 5.5% (in water phase)

Compared with molecular solubility in a mixture of water and 6% triethanolamine alone — 3.9%

Compared with molecular solubility in water alone 0.07%

It will be seen that sulfathiazole in the emulsion has a molecular solubility 800 times greater than in water, due, by inference, to the triethanolamine. The experiment indicates that 2% triethanolamine dissolved in the water phase of the emulsion holds a molecular solution of sulfathiazole in the emulsion of over 5%. Since the emulsion contains 24% of watery phase, and this watery phase holds 5.5% of sulfathiazole, then the total sulfathiazole in solution in 100 Gm. of the emulsion is $24 \times 5.5 = 1.32$ Gm., which, in turn, represents 26% of the total sulfathiazole present in the emulsion.

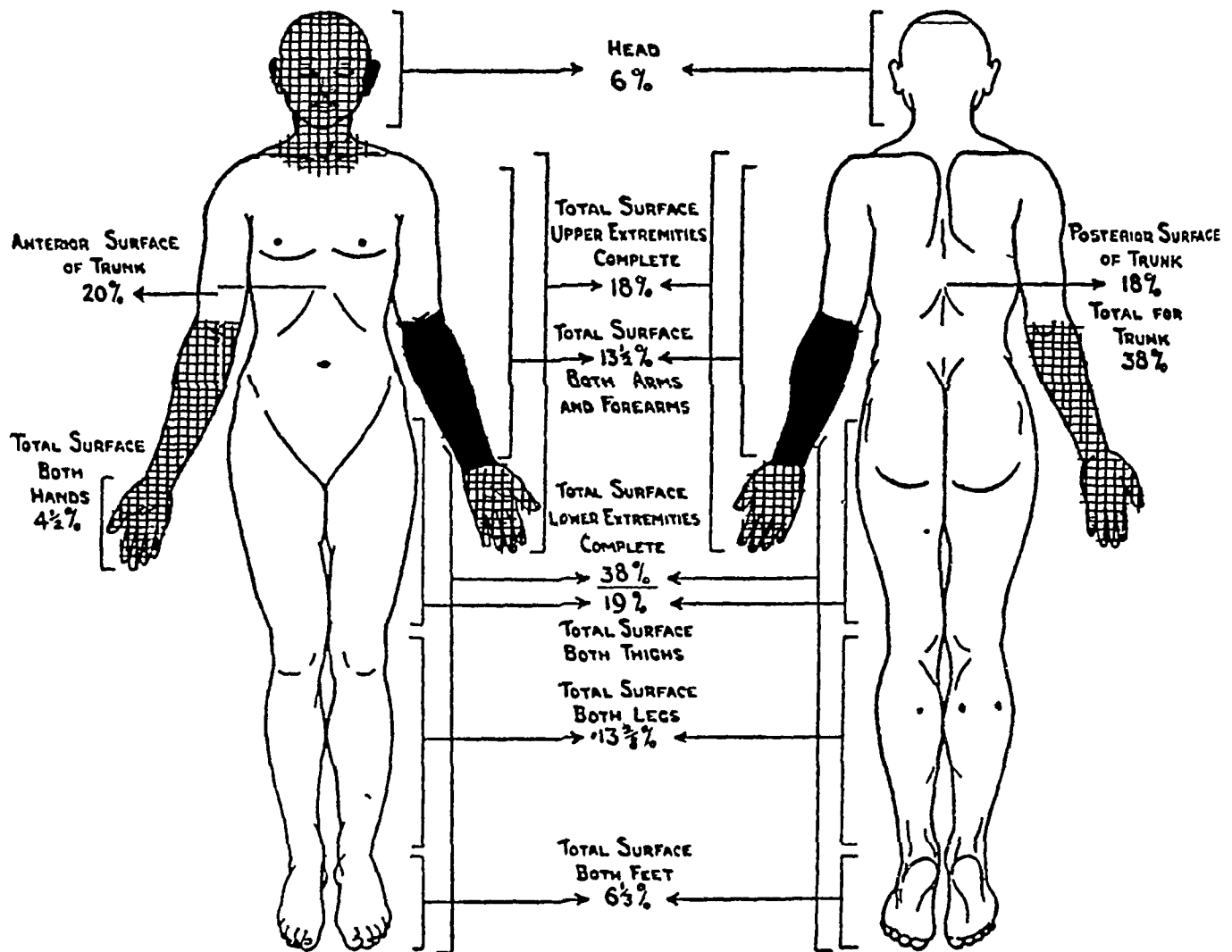
From the above experiments it will be seen that the 5% M G H emulsion, while allowing for a remarkably high molecular concentration of sulfathiazole, actually has a very satisfactory and prolonged curve of delivery into the adjoining tissues. These experimental and clinical results indicate the superiority of an emulsion base over ordinary ointment bases.

GRAFTING OF BURNED AREAS

How Organized Timing Permits Early Skin Grafting

Modern burn treatment aims at an assessment of the burn damage as soon as shock and toxemia have passed, and the immediate start of reconstructive procedures. Tannic acid eschar and effective shock treatment have lowered burn mortality; now, early skin grafting is reducing burn morbidity. The patient is no longer allowed to suppurate in granulations and eschars for weeks and months while poor and useless skin is coaxed from burn margins, sweat glands, and hair follicles. The burn wounds are surfaced with the patient's own skin as soon as feasible. With these thoughts in mind, efforts have been directed in the Montreal General Hospital, toward the early preparation of burned areas for grafting.

By early grafting we mean grafting as close to the burn-time as the patient's condition will permit. Theoretically, and from the skin grafting viewpoint, this would be about the 6th or 7th day, when the postburn perivascular edema in the subepidermal and subcutaneous layers is subsiding. Practically this conflicts with the toxemic phase, and we are usually unable to apply our grafts, in burns of any extent, until the 14th day onward. However, we feel there is an optimum time for grafting, and that it is early, before granulations have formed to any extent. As time goes on the granulations increase, grafting is less certain, and the resultant subgraft scar detracts from the final result.



CHILDREN

Degree of Burn

Lower Extremities	38 - twice (12 - age)
Trunk	38 + half (12 - age)
Head	6 + (12 - age)
Upper Extremities	18 + half (12 - age)

ESTIMATION OF TOTAL AREA BURNED 20% OF BODY

Summary

Face—all, 2nd degree
 Left ear—possibly 3rd degree
 Forearms } Right, all 2nd degree
 Wrists } Left, largely 3rd degree
 Hands—all 2nd degree

1st Erythema

2nd Partial destruction

3rd Complete destruction

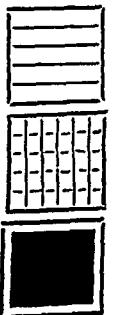


CHART 1A (See Chart I opposite)

From a reconstructive point of view, any burn dressing that permits easy removal and inspection at the end of 6, 8 or 10 days, or even earlier, is the ideal dressing. This is especially so on the critical areas, such as face and flexor surfaces, where contractures are so liable to ensue. Saline baths and dressings permit such inspection from the first, but, in our experience, have been cumbersome and impractical. The eschars, at present in use, do not permit such inspection. To date, sulfathiazole emulsion dressings of these critical areas have proven eminently satisfactory and the foregoing wide-mesh ("sulfamesh") gauze technique has been worked out. Contrary to the opinions of Blair and Brown,¹⁰ and Brown and McDowell,^{11, 12} that a wide-mesh gauze is a painful dressing and permits granulations to grow up through the mesh, we have not found it so, and feel the wide-mesh strands provide a mechanical factor, "splinting" or "snubbing" the wound surface, providing a more secure dressing, with better drainage, and is just as easily and painlessly removed as is fine-mesh gauze.

The burned areas are "papered" with 4 x 6 inch sheets of "sulfamesh." This clings snugly to the wound surface. A liberal coating of sulfathiazole emulsion is applied and dressing built up with gauze-cuts and cotton waste, as recommended by Brown and McDowell,¹² for a pressure dressing. A few days of such treatment, with change of dressings at three-day or longer intervals, and the area is ready for grafting. Earlier in our experience dressings were changed to saline soaks 24 hours before grafting, fearing the emulsion might interfere with the "take." Apparently this is not so, for the emulsion dressing is now removed in the operating room and the graft applied without further preparations, notwithstanding a fairly heavy sulfathiazole content of the underlying tissues.

Our grafts are of the split variety, half or three-quarter thickness, cut with the Padgett dermatome. These are transferred to "sulfamesh" gauze and sewn in with the gauze. The wide-mesh gauze, again, provides an excellent mechanical factor, and even more so with the thin layer of cement still adherent on the skin from the dermatome. With the aid of a basting suture it "snubs" the graft well into position, with little chance of movement. The dressing is built up with wisps of absorbent cotton wrung out of sulfathiazole emulsion, packed tightly against the "sulfamesh" and covered over with the gauze-cuts and cotton waste.

Split grafts, with this technique, have been uniformly satisfactory. In our hands, the "pinch graft" has been relegated to the sidelines, except where insufficient normal skin exists.

The immediate grafting of burns, as suggested by Gillies during his recent tour, is interesting, but practical only for the small, deep and definite burns. Then, as Gillies says, the burn can be "cut away" and the resulting surgical wound grafted. It is impractical in larger burns, where shock and toxic phases would prohibit such surgery.

One might summarize the salient points and reasons for the early grafting of suspected or definite deep skin burns as follows: (1) The surface is

fresh and firm, with thin granulations or beginning granulations, which will result in a minimal layer of scar tissue in the subgraft area (2) These early surfaces are in an optimum phase for grafting As the granulations age, they tend to become exuberant and less certain for graft "take" and may have to be shaved away (3) The grafting is clinically beneficial to the patient, as dressings and open surfaces are early done away with (4) Infection is controlled early with sulfathiazole emulsion (5) Any slough can be removed surgically just prior to putting on the graft (6) It does no harm to cover up small "probable" islands of regenerating epidermis They will at best provide a poor epithelium, at a slow rate (7) If the patient is left with granulating areas for a long time he tends to become anemic and a less suitable recipient for his own grafts (8) At about the fourteenth day the patient's general condition is usually at its optimum phase

Regarding those cases in which tannic acid-silver nitrate eschar has been used, certain comments are necessary All blebs require removal and treatment with the emulsion One must be constantly on guard to recognize infection under the tan, and to provide adequate drainage After the fourteenth day removal of the tannic, or any other, eschar is desirable, for early grafting of resultant raw surfaces Usually a tannic acid eschar is beginning to separate at such time In this connection, our experience with gentian violet or triple dye eschars has been that they seem to have become organized with the underlying tissues, and having penetrated them, are removable only through suppuration or surgery

OBSERVATIONS ON THE PATHOLOGY OF BURNS

It is not our intention to enter into a full discussion of the pathology of burns For this, reference may be made to the excellent papers by Brown and McDowell,¹² and by Wilson, MacGregor and Stewart³⁶ We do wish, however, to make some general remarks upon the degree and healing of burns and to illustrate certain points in relation to skin grafting in cases treated with sulfathiazole emulsion

Skin is a highly specialized structure composed of the epidermis and its appendages, and the tough fibro-elastic derma well vascularized and innervated It is this tough elastic derma that forms the admirable bearing pad and a suitable underlay for the proper development of the epidermis

In the local treatment of burns it is highly desirable to have the defect reconstituted, as nearly as possible by normal skin, in order to give a good functional surface and to prevent deformities

The failure to attain this result is due to one thing, namely, the organization of granulation tissue into scar tissue It is scar tissue that produces contractures It is the epidermization of scar tissue that produces the poor-bearing surface of hyperkeratotic "scar skin" (Fig 6) that binds, shortens, cracks, peels under the every day trauma of ordinary activity, and is useless as a bearing surface for labor It is stiff and devoid of elastic tissue, is poorly vascularized, and poorly innervated The epidermal appendages are



Fig 6

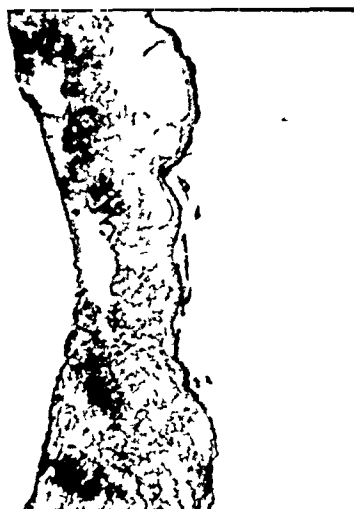


Fig 7



Fig 8

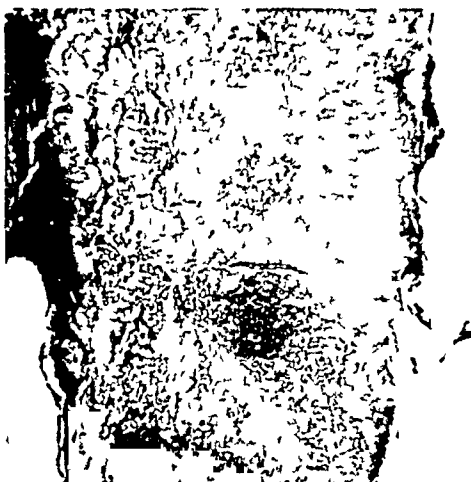


Fig 9



Fig 10



Fig 11

Fig 6—"Scar skin" in deep skin burn on the dorsum of the hand treated by trinitic acid. Biopsy taken eight months after the accident, while the scar skin was being removed in preparation for skin grafting. At the base of the section there is a thin layer of preexisting skin with sweat glands. This is overlaid by a dense thick scar which is covered by a uniform layer of epidermis, without papillae. On the surface of the epidermis there is a very thick layer of keratin. Note the well developed sweat gland duct extending from the epidermis through the scar toward the nest of sweat glands at the base of the section.

Fig 7—Regeneration of epidermis from a hair follicle in a superficial burn treated with sulphathiazole emulsion. Biopsy taken on seventh day. Note the epidermis spreading out from the broad follicle in the center of the section.

Fig 8—Four day old infected burn. Biopsy taken on ninth day, after five days' treatment with sulphathiazole emulsion.

Fig 9—Deep skin burn at 26 days—treated with sulphathiazole emulsion.

Fig 10—Junction of ungrafted area 60 days old. Skin graft 34 days old on the site from which the biopsy shown in Figure 9 was taken.

Fig 11—Deep skin burn at 50 days—treated with sulphathiazole emulsion.

few or absent. The presence of too much scar tissue underlying a skin graft robs it of much of its good functional result.

Regeneration of the epidermis of burned skin takes place from viable epithelium in the area, i.e., from the margins of the wound, from hair follicles (Fig. 7), ducts of sweat glands (Fig. 9), and epidermis that has escaped complete destruction in the burned area. It is obvious that if the whole thickness of the skin is destroyed the only possible source of restitution of the epidermis is from the margins of the wound.

Healing by granulation tissue usually goes on to scar tissue formation, but in partial damage of the derma if epithelization is rapid enough, the granulation tissue appears to resolve and is replaced by reconstituted elastic derma.

The healing of burns, then, resolves itself into a race between granulation tissue formation and the regeneration of the epidermis. Upon the outcome of this race will depend the necessity or not of grafting.

Infection inhibits epithelization, and further destroys the skin and favors granulation tissue, so that the control of infection is of great importance.

Burns, from the point of view of healing, fall into two classes: (1) Those that reestablish good skin and do not require grafting; (2) Those that fail to heal, or heal by scar skin and will require grafting.

In these classes there are two extremes that are at once obvious. First, the very mild burn, in which the epidermis is not completely destroyed. Restitution is rapid. Second, very deep burns, which obviously extend beneath the derma. Healing is always by epithelization of scar tissue, and if the wound is large enough, grafting will be necessary.

Between these two extremes lie the problem cases, in which it is often difficult, on first observation, to determine the depth of the burn. Very often the depth of destruction is not uniform, so that it is not easy to predict how many possible sources of epithelial regeneration remain, or just what reaction the wound will follow. Time is required to settle this question. Usually, it can be pretty well determined at the time of the first dressing at the end of one week.

In those cases in which only the epidermis has been destroyed, or where the derma is involved only superficially, epithelization will be found complete, or nearly so, at the time of first dressing is done. There is usually some persisting inflammatory cellular exudate about the vessels.

Figure 8 represents a four-day-old infected burn, which has extended into the papillary zone of the derma. The biopsy was taken on the ninth day, after five days' treatment with sulphathiazole emulsion. Epithelization was almost complete. Note the tapering layer of epidermis which extends from a hair follicle just out of the field to the left. The derma is intact, with no granulation tissue on the surface. The epithelium is being applied directly upon the elastic derma. There is an overlying thin layer of coagulated exudate which has slightly separated. There is no edema, and only a mild perivascular cellular exudate of lymphocytes and eosinophils.

Where the burn has extended deeper, destroying the more superficial hair follicles and perhaps some of the sweat glands, the inflammatory reaction is much more intense, granulation tissue is more abundant, epithelial regeneration is slower in making an appearance, and the foci of new epidermis will be fewer in number.

Figure 9, taken on the twentieth day from the case reported herein, illustrates this degree of burn. At the base of the section there is intact viable derma containing many sweat glands. This is overlaid by a layer of granulation tissue containing areas of intense inflammatory cell infiltration, fragmented elastica, some foreign body giant cells about debris of epithelium, and of hairs left naked by destruction of the epithelial cells of the follicle. Lying perpendicularly, about the centre of the section, can be seen a regenerated sweat gland duct which, in the many sections taken, could be traced to the surface, where there is a small island of regenerating epidermis. On the surface there are ragged fragments of coagulated exudate. In other fields of this section, somewhat larger islands of epidermis were seen extending out from viable follicles.

Skin grafts were applied at this stage to part of this wound, as it was apparent that epidermization would be a very prolonged process, and scar tissue would form long before it could be completed, resulting in "scar skin" as in Figure 6.

At 40 days, another area was grafted, and at 66 days, when the remainder of the area was to be grafted, a biopsy was taken through the first graft, 34 days after its application, and the adjoining ungrafted area. Figure 10 shows the junction of the ungrafted area and the first graft. There is a marked increase in the granulation tissue in the ungrafted area. The grafted area shows a remarkable transformation. The graft and the skin layer of original derma are joined by a narrow zone of young fibrous tissue, in which there are a few foci of lymphocytes and some foreign body giant cells about groups of epithelial cells. Most striking is the effect upon the damaged granulating skin by the application of the graft. No paring was done.

Figure 11 represents a section from another burned area in the same man as in Figures 9 and 10, at 50 days. The section, stained with Weigert's elastic tissue technique, shows subcutaneous tissue, and a very narrow strip of derma, represented by the dark-staining elastica at the base. There are no viable sweat glands or hair follicles and no evidence of epithelial regeneration in this section. Overlying the thin layer of derma is a thick, irregular layer of granulation tissue showing marked inflammatory cell infiltration and areas of edema. Although the derma is not completely destroyed one could not expect much of epithelial regeneration. Skin grafting was done at this stage after paring down this type of excessive edematous granulation tissue, which is not a satisfactory bed for the reception of a graft.

ILLUSTRATIVE CASE HISTORY

Case Report—M G H O G, male, age 70, was admitted, May 28, 1942, about two hours after a severe flash burn of the face, neck, both forearms and hands. An accurate estimate of the area and depth of burn will be found on the accompanying burn chart. In this connection, it should be noted that two weeks elapsed before it could be definitely decided that the left forearm required skin grafting.

On admission, the patient was in moderate shock, clinically, and appropriate measures were instituted. Local treatment was carried out with sulfathiazole emulsion and pressure dressings, according to our timing chart. The details of this and the details of his general course during the first four days will be found on the burn chart in some detail. Certain points about this period, as noted on the chart, deserve special comment. In the first place, the shock was controlled by plasma, *etc.*, though at the 10- to 18-hour period, with some difficulty. This was occasioned by the difficulty with the continuous drip, which infiltrated, and through a misunderstanding was discontinued for three hours. On rectifying this, when the hemoconcentration was reported, no further trouble occurred during the shock period. This serves to illustrate forcibly, and we have unfortunately had other such confirmation, the necessity of maintaining a 24-hour service by the shock team. At 45 hours, after apparently being well controlled, a definite toxemia phase developed quite suddenly, with fever, rapid pulse, restlessness, irrational mental state, partial suppression of urine and rapid fall in hemoglobin. With the administration of intravenous glucose this condition rectified itself in about 15 hours. Following this period, there will be noted a rapid return to relative normality in all recordings and in his general condition.

The patient's subsequent course was uneventful and without any infection, although the depth of the burn on his left forearm was only determined after two weeks. Even at this time it was determined with some difficulty, since many epithelial islands were evident. A further delay of 10 days ensued, as Doctor Gerrie was out of town. On the 26th day split-grafts were placed *in situ* without any special preparations, and 100% "take" ensued. There is no functional disability.

During the skin-grafting period biopsy studies were made before and after grafting, the interesting results of which are referred to in the section on pathology.

BIBLIOGRAPHY

- ¹ Ackman, Douglas, and Wilson, Gordon. *Can Med Assn Jour*, **46**, 209-214, 1942.
- ² Ackman, Douglas, and Wilson, Gordon. *Can Med Assn Jour*, **47**, 1-7, 1942.
- ³ Allen, H. S. *Jour Amer Med Assn*, **116**, 1370-1373, 1941.
- ⁴ Allen, H. S., and Koch, S. L. *Surg Gynec & Obst*, **74**, 914, 1942.
- ⁵ Alldrich, R. H. *New Eng Jour Med*, **208**, 299-309, 1933.
- ⁶ Berkow, S. G. *Arch Surg*, **8**, 138-148, 1924.
- ⁷ Bettman, A. G. *Northwest Med*, **34**, 46-51, 1935.
- ⁸ Blalock, A., and Mason, M. F. *Arch Surg*, **42**, 1054-1059, 1941.
- ⁹ Rose, B., and Browne, J. S. L. *ANNALS OF SURGERY*, **115**, No. 3, 390-399, 1942.
- ¹⁰ Brown, J. B., Blair, V. P., and Byars, L. T. *Amer Jour Surg*, **43**, 452-457, 1939.
- ¹¹ Brown, J. B., Byars, L. T., and McDowell, F. *ANNALS OF SURGERY*, **40**, 1192-1210, 1940.
- ¹² Brown, J. B., and McDowell, F. *Clinics*, **1**, No. 1, 25-36, June, 1942.
- ¹³ Bunyan, J. *Brit Med Jour*, **2**, 1-7, 1941.
- ¹⁴ Cannon, W. B. D. Appleton & Co., New York, 1923.
- ¹⁵ Collier, F. A., and Maddock, W. G. *Jour Amer Med Assn*, **99**, 875, 1932.
- ¹⁶ Davidson, E. C. *Surg Gynec & Obst*, **41**, 202-221, 1925.
- ¹⁷ Davis, J. S. *Amer Jour Surg*, **47**, 280-298, 1940.
- ¹⁸ Farmer. Read at the American Assn Surg Trauma, Boston, June, 1940. (In press).
- ¹⁹ Harkins, H. N. *Clinics*, **1**, No. 1, 25-36, 1942.

- 20 Medical Research Council War Memo No 1 Treatment of Wound Shock, September, 1940
- 20a Medical Research Council Bulletin War Medicine, 1, No 4, 209-210, 1941
- 20b Medical Research Council Bulletin War Medicine, 2, No 1, 16-24, 1941
- 21 Moon, V H Shock and Related Capillary Phenomena, New York, Oxford University
- 22 Mowlen Proceedings Royal Society Section on Orthopedics, 34, No 4, 221-224, 1941
- 23 Oldfield Univ of Leeds Mag, 1, No 2, 11-21, 1941
- 24 Owen, Neal Personal communication
- 25 Padgett, G C Surg Gynec & Obst, 69, 779-793, 1939
- 26 Pickrell, K L Bull Johns Hopkins Hosp, 69, 217-221, 1941
- 27 Rhoads, J E, Wolff, W A, Saltonstall, H, and Lee, W E Clinics, 1, 37-42 1942
- 28 Scudder, J Shock Blood Studies as a Guide to Therapy, Phila, J B Lippincott Co, 1940
- 29 Siler, J C, and Reid, Mont R ANNALS OF SURGERY, 115, 1106-1117, 1942
- 30 Taylor, F J A M A, 106, 1143-1145, 1936
- 31 Wakeley, C P G, *et al* Proc Royal Soc Med—T1 Sect Sections of Surg, Therap and Pharmacol, 34, 43-72, 1940
- 32 Wakeley, C P G Surgery, 10, 207-232, 1941
- 33 Wallace, A B The Treatment of Burns Oxford War Manual
- 34 Weil, P G Can Med Assn Jour, 46, 3-7, 1942
- 35 Weil, P G, and Meakins J C Clinics, 1, No 1, 59-67, June, 1942
- 36 Wilson, W C, MacGregor, A R, and Stewart, C P Brit Jour Surg, 15, 826-865, 1937-38
- 37 Drew, C R Anaesthesiology, 3, No 2 176-194, 1942
- 38 Vivino, J J, and Spink, W W Proc Soc Exp Biol and Med, 49, 336-338, June, 1942

A STUDY OF THE "SHOCK-DELAYING" ACTION OF THE BARBITURATES

WITH A CONSIDERATION OF THE FAILURE OF OXYGEN-RICH ATMOSPHERES TO
DELAY THE ONSET OF EXPERIMENTAL SHOCK DURING ANESTHESIA

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IT HAS BEEN SHOWN REPEATEDLY that there is a concentration of the cellular elements of the blood under ether and a dispersion of them under various barbiturates, the blood has thus been described as concentrated under ether and "diluted" under barbiturates. Because of these and other observations, Seeley, Essex and Mann¹⁵ (1936) set out to determine by experiment whether the onset of traumatic shock would occur after the same interval under ether as under a barbiturate. A first step in their work was to develop a "standard method" of producing trauma.

We have repeated this work, insofar as their two major groups of dogs are concerned. The possibility that barbiturates will delay the onset of shock is of great importance if it is applicable to the shock problem in general, and of considerable importance if this effect can be shown to hold even under special circumstances. We have examined the effect of a barbiturate and compared it with ether in circumstances where shock is produced by bleeding. We have also studied the effects on "shock-time" of respiration of room air compared with oxygen-rich atmospheres under the conditions of these experiments.

METHODS—*Experimental Animals* Forty mongrel dogs were used in this study.

Anesthesia—A freshly prepared 5% solution of sodium amytal was injected into the saphenous vein in an initial dose of 50 mg per Kg. Ether was induced in a closed cabinet and then maintained as described by Hardenbergh and Mann⁷ (1927) in order to repeat the experiments of Seeley, Essex and Mann. Particular effort was made to maintain comparable levels of anesthesia under the two anesthetics. The level chosen was that in which the corneal reflex persisted but was very sluggish. In about half of the experiments of each group the level of anesthesia was controlled further by means of comparable records of the flexion reflex of the leg when the central end of the cut sciatic nerve was stimulated by a Grass stimulator (condenser type), see Beecher and Moyer,³ 1941.

The Production of Shock—The intestinal manipulation experiments were carried out as described by Seeley, Essex and Mann (1936). They produced trauma in the following way: "The entire length of small intestine was delivered outside the abdominal cavity and gently manipulated by a continuous rolling motion between the hands of the operator. After 30 minutes of manipulation the intestines were spread out on towels on the anterior abdominal wall. The intestines were turned every 30 minutes to remove fibrin and to avoid unequal exposure of the loops. The blood pressure in the femoral artery was recorded at intervals on a standard kymograph. When the blood pressure had declined to a level of 70 Mm. of mercury, the animals were considered to be in a state of shock." Blood concentration studies were made.

In the bleeding experiments which we carried out, the first blood was drawn from the femoral artery as soon as the control samples and measurements had been taken. The first hemorrhage amounted to 10% of the body-weight. Thirty minutes later a second hemorrhage of 0.5% body-weight was carried out. Every half-hour following this, until death, blood to the extent of 0.25% body-weight was withdrawn.

"Shock-time" was measured from the beginning of intestinal manipulation, or in the bleeding experiments from the beginning of bleeding, until the mean arterial blood pressure had fallen to 70 Mm. Hg and had remained at this level or below for one-half hour. "Death-time" was measured from the beginning of intestinal manipulation, or from the beginning of bleeding in the bleeding experiments, until death occurred.

Blood Data—Mean arterial blood pressure was determined and recorded through a cannula placed in the femoral artery. Hematocrit determinations in the bleeding experiments were made by the method of Sanford and Magath¹³ (1929) on 6 cc. arterial samples. Blood withdrawn routinely in the course of the experiment was utilized for this determination. In the intestinal manipulation experiments the hematocrit was determined on 1.25 cc. venous blood by the method of Rourke and Einstene¹² (1930). Serum protein measurements were made with the Zeiss refractometer. This instrument had been repeatedly checked against Kjeldahl protein determinations. Arterial and venous blood oxygen measurements were made by the method of Van Slyke and Neill¹⁹ (1924). When ether was present in the blood the modifications of Shaw and Downing¹⁶ (1935), and Snyder¹⁷ (1938) were used in determining oxygen content of the blood.

RESULTS—The data of Table I have been compiled from the results of Seeley, Essex and Mann. Tables II and III present our results on repetition of the same experiment. It can be seen that in the case of the ether shock time we are in remarkably close agreement. Our data differ from theirs by

* Parsons and Phemister¹⁰ (1930) used exposure and repeated manipulation of the intestine to produce shock, apparently under barbiturates and ether, but they record few details of their study.

only 5% * It is worth observing that in this case both groups had the same number of experiments, seven In the case of the sodium amytal (alone) experiments we had the same number of experiments as with ether, seven, while Seeley, Essex and Mann had three Possibly this may account in part at least for our failure to agree better with their amytal data A further explanation probably lies in depth of anesthesia Seeley, Essex and Mann gave, apparently, a single initial injection of the barbiturate without later supplement †

TABLE I
DATA COMPILED FROM ARTICLE BY SEELEY ESSEX AND MANN¹⁵

Anesthetic Agent	Number of Dogs	Time for Shock to Develop Hrs	Death Time Hrs
Ether alone	7	Average 3 88	Average 5 88
Sod amytal alone 50 mg /Kg	3	Average 11 55	Average 14 73
Sod amytal 25 mg /Kg preceding ether	5	Average 10 50	Average 13 50
Ether followed by 25 mg /Kg sod amytal	2	One animal 6 42 One animal 11 42	One animal 10 25 One animal 15 08

TABLE II
SHOCK BY INTESTINAL MANIPULATION
Ether and Room Air

No	Wt Kg	Sex	Shock- Time Hrs	Death- Time Hrs	Hematocrit		Serum Protein	
					Control %	Shock %	Control %	Shock %
1	7 2	♀	10 25	14 17	50 0	69 4	6 94	6 34
2	7 9	♀	1 00	4 83	56 6	67 6	6 90	7 13
3	11 0	♂	8 16	10 33	56 3	66 1	7 93	7 61
4	8 8	♀	4 91	5 55	57 7	70 4	7 70	6 90
5	12 6	♂	2 28	8 58	50 0	60 4	6 68	6 75
6	12 2	♂	1 00	5 16	47 0	69 0	6 25	7 70
7	8 8	♂	1 00	1 50	55 1	80 8	7 11	7 91
Average			4 09	7 16	53 2	69 1	7 07	7 19
			4 1 ± 1 5		7 2 ± 1 6			

* This should dispose of any possible objections that differences between the average room temperatures, mean barometric pressures, or mean relative humidities would, in altering evaporation rates, make it impossible to compare data obtained in these different parts of the country It is our policy to observe and record such data twice daily, in the middle of the morning and in the middle of the afternoon These factors are too often neglected A further control on this point is the fact that both types of experiments, ether and barbiturate, were made in each place, so differences between the two should emerge, if present

† A recent letter from Dr Mann supplied the following information "While in our original article we presented the data on only three dogs in which amytal was used, before the paper was published we had enlarged the number and to date have a fairly large series We failed to state in the article that occasionally it was necessary to give small amounts of amytal when the animal became light, until shock had developed It is also our practice to decrease ether as soon as the animal is definitely in a condition of shock (suggested by Meltzer) so that the time of action of the two anesthetic agents does not differ greatly"

TABLE III
SHOCK BY INTESTINAL MANIPULATION
Sodium Amytal and Room Air

No	Wt Kg	Sex	Shock- Time Hrs	Death- Time Hrs	Hematocrit		Serum Protein		Na Amytal mg /Kg		
					Control %	Shock %	Control %	Shock %	Initial	Suppl	No Inject
8	9 8	♀	11 41	14 83	32 3	57 2	7 13	8 33	51	5 1	2
9	18 6	♂	9 00	15 58	39 6	62 6	7 13	7 72	51	24 8	18
10	6 8	♂	9 16	10 30	40 4	52 0	6 20	6 18	50	14 7	5
11	8 5	♂	2 17	5 83	37 6	46 5	6 66	6 10	50	19 4	5
12	11 0	♂	9 00	18 50	39 8	60 2	7 89	8 18	50	30 0	16
13	8 4	♂	10 50	11 16	40 4	74 8	7 09	7 70	50	11 3	4
14	28 4	♂	6 58	8 90	53 8	67 3	—	—	50	30 0	6
Average			8 26	12 16	40 6	60 1	7 02	7 37	50	19 3	8
			8 3 ± 1 2	12 2 ± 1 7							

In our experience, it was not possible to maintain a level of barbiturate anesthesia that was comparable with that of the ether experiments by this single injection (except in one out of 20 amytal experiments). In our experiments, following this initial injection, sometimes sooner than an hour, the animal's anesthesia would become very light, so that the dogs could not truly be considered as anesthetized unless supplementary doses of barbiturates were given. It seems to us that Seeley, Essex and Mann were comparing ether anesthesia with, in the latter part of their barbiturate experiments, a state in which hardly any anesthesia produced by the drug itself was present, but what depression there was was chiefly the depression of the shock state. We have made particular efforts to maintain comparable levels of anesthesia. Because of the larger number of our amytal experiments and the particular efforts we have made to maintain comparable levels of anesthesia in the two groups we are inclined to believe that our values more nearly express, than does the other series, the shock-delaying properties of the barbiturates. Shock was delayed twice as long under barbiturates as under ether (our data) rather than three times as long (Seeley, Essex and Mann). There is no point in dwelling on this quantitative difference, of much more importance is the fact that we confirm their observation that the barbiturates *under the conditions of this experiment* do delay the onset of shock, and that death will occur later if barbiturate anesthesia be used than if ether is the agent employed.

We next set out to test whether or not barbiturates would delay the onset of shock produced by bleeding, with the belief that this might help to round out the picture of possible usefulness of the agents in seriously wounded individuals. From Tables IV, V, VI and VII it is apparent that no significant shock-delaying action has been demonstrated when hemorrhage constitutes the trauma.

We had planned to compare the effects of barbiturates and ether in muscle trauma experiments but decided not to, in view of the failure of barbiturates to delay shock produced by bleeding in our experiments and the failure of barbiturates to delay, in comparison with ether, the shock produced in the muscle trauma experiments of Parsons and Phemister,¹⁰ and of Bla-

lock⁴ Parsons and Phemister (1930), in a large series of experiments (70) upon anesthetized dogs, studied the effects of stimulation of the nerves of the limb, of traumatization of the limb, and of bleeding. For anesthetics they employed ether and morphine in 24 cases, ether alone in 17 cases, morphine and barbital in 18 cases, and barbital alone in 11 cases. They report that except where morphine was used, the effects under ether or barbiturate were very similar.

TABLE IV
SHOCK BY HEMORRHAGE
Ether with Room Air

No	Wt Kg	Sex	Shock- Time Hrs	Death- Time Hrs	Hematocrit		Serum		Protein		Arterial O ₂ Content		Venous O ₂ Content	
					Control %	Shock %	Control Gm %	Shock Gm %	Control Gm %	Shock Gm %	Control Vols %	Shock Vols %	Control Vols %	Shock Vols %
1	6.4	♂	4.50	4.85	42.1	30.5	7.96	6.19	13.7	10.4	6.0	2.9		
2	9.7	♀	2.05	4.32	51.9	39.8	6.64	5.18	19.9	16.8	6.2	4.7		
3	8.0	♀	4.00	5.09	51.8	36.8	6.55	5.45	18.1	13.4	10.8	1.8		
4	8.2	♀	1.50	2.00	49.4	41.5	6.77	5.56	18.9	14.0	8.8	2.1		
5	6.0	♀	1.63	2.67	58.9	51.5	7.22	5.94	19.0	18.5	12.0	8.6		
6	7.0	♀	1.67	4.57	46.9	43.4	6.89	5.90	18.1	16.7	16.8	9.1		
Average			2.56 2.6 ± 0.6	3.92 3.9 ± 0.5	50.2	40.6	7.01	5.70	18.0	15.0	10.1	4.9		

TABLE V
SHOCK BY HEMORRHAGE
Ether with 100% Oxygen

No	Wt Kg	Sex	Shock- Time Hrs	Death- Time Hrs	Hematocrit		Serum		Protein		Arterial O ₂ Content		Venous O ₂ Content	
					Control %	Shock %	Control Gm %	Shock Gm %	Control Gm %	Shock Gm %	Control Vols %	Shock Vols %	Control Vols %	Shock Vols %
7	11.0	♂	0.50	1.08	45.3	42.8	6.89	6.62	—	—	—	—	—	—
8	7.3	♀	4.18	4.49	59.1	44.0	5.88	4.16	24.8	19.8	19.1	7.9		
9	7.0	♂	4.40	4.45	45.6	35.1	7.50	5.79	19.3	15.2	13.1	5.0		
10	7.8	♂	4.33	4.44	52.0	43.7	7.07	5.72	19.0	15.7	14.4	7.3		
11	9.0	♂	4.05	4.48	63.3	52.9	8.08	5.70	26.6	23.6	21.0	13.2		
12	12.5	♂	2.75	3.68	58.6	51.1	6.73	5.58	24.6	21.8	16.5	14.4		
13	9.2	♀	3.00	6.77	60.6	55.0	7.68	6.27	24.2	22.6	23.8	13.3		
Average			3.32 3.3 ± 0.5	4.20 4.2 ± 0.6	54.9	46.4	7.12	5.69	23.1	19.8	18.0	10.2		
Combined ether Average			2.8 ± 0.4	4.1 ± 0.4										

TABLE VI
SHOCK BY HEMORRHAGE
Sodium Amytal with Room Air

No	Wt Kg	Sex	Shock- Time Hrs	Death- Time Hrs	Hematocrit		Serum Protein		Na Amytal mg /Kg		Arterial O ₂ Content		Venous O ₂ Content	
					Con- trol %	Shock %	Con- trol Gm %	Shock Gm %	Initial mg	Suppl mg	Con- trol Vols %	Shock Vols %	Con- trol Vols %	Shock Vols %
14	8.6	♂	1.55	—	35.6	33.8	6.98	5.97	50	0	14.0	14.1	10.6	6.0
15	11.0	♂	4.90	—	29.1	28.6	5.46	4.94	50	41	11.0	11.1	5.9	1.6
16	11.8	♀	4.72	—	38.4	32.9	7.27	6.12	50	13	11.4	13.0	7.4	2.0
17	8.5	♀	1.55	—	39.4	39.2	4.96	4.05	50	12	14.2	16.0	9.6	8.2
18	12.2	♀	0.75	1.58	38.9	54.7	6.49	6.32	50	8	14.9	18.8	9.1	1.6
19	10.7	♂	5.00	7.38	42.7	53.8	6.05	5.34	56	15	15.8	20.1	9.0	2.2
20	11.2	♀	5.50	6.53	43.7	42.7	5.90	4.81	54	12	17.7	17.3	15.5	5.6
Average			3.42 3.4 ± 0.8	5.16	38.0	40.8	6.16	5.36	51	14	14.1	15.8	9.6	3.9

"SHOCK-DELAYING" ACTION OF BARBITURATES

TABLE VII
SHOCK BY HEMORRHAGE
Sodium Amytal with 100% Oxygen

No	Wt Kg Sex		Shock- Time Hrs	Death- Time, Hrs	Hematocrit		Serum Protein		Na Amytal mg /Kg		Arterial O ₂ Content Con- trol %	Venous O ₂ Content Con- trol %		Shock Vols %	Shock Vols %
					Con- trol %	Shock %	Con- trol Gm %	Shock Gm %	Initial	Suppl Inject		Shock Vols %	Shock Vols %		
21	9 0	♀	4 50	5 36	42 9	38 8	7 57	6 68	50	47 11	18 7	16 5	10 1	2 8	
22	9 0	♀	3 00	6 60	44 0	48 0	7 11	5 70	55	24 8	19 6	21 8	14 7	9 6	
23	7 0	♀	0 50	6 77	43 7	53 4	5 05	4 73	54	20 6	18 7	22 7	12 5	7 0	
24	9 7	♀	2 50	6 07	37 9	37 1	5 53	4 51	54	16 7	13 7	16 6	9 8	6 2	
25	8 2	♀	4 00	5 67	43 0	42 7	7 27	6 14	54	28 13	15 8	15 3	14 5	6 5	
26	8 0	♂	4 50	5 20	32 4	39 4	6 93	6 01	52	18 8	14 0	16 6	11 8	5 7	
Average			3 17	5 95	40 7	43 2	6 58	5 63	53	26 9	16 8	18 3	12 2	6 3	
			3.2 ± 0.6	6.0 ± 0.3											
Combined															
Na amytal															
Avg			3.3 ± 0.5	5.7 ± 0.6	39.3	41.9	6.35	5.49	52	20 6					

Blalock (1942), in his study of the comparison of the effects of the local application of heat and cold in the prevention and treatment of shock produced by pounding an extremity, records among other data the following when heat was added to the injured member (Table VIII)

TABLE VIII

Anesthetic Agent	Nembutal	Barbital	Morphine and Ether
Number of dogs	14	6	5
Avg diff in wt of traumatized and nontraumatized parts, in per cent body-wt	3.80	4.05	3.40
Death-time	5° 52'	5° 44'	5° 50'

It is clear that the barbiturates do not prevent in comparison with morphine and ether the loss of fluid into the traumatized extremity, under the conditions of this experiment, nor do they delay the death-time over that produced under morphine and ether. Therefore, considering our hemorrhage data, and Parsons and Phemister and Blalock's muscle trauma data, we have not continued with the traumatization of limb experiments.

Conflicting reports have been made concerning the usefulness of oxygen in shock. We wished to test whether or not breathing of an oxygen-rich (about 100%) atmosphere would be of value in delaying shock under conditions where these two widely different types of anesthesia were employed. From the data, it is apparent that it is possible nearly to double the venous oxygen,^{*} and yet we do not find any significant delay in the onset of shock as a result of using an oxygen-rich atmosphere. Since this was so, we have combined the high oxygen and the 100m air data.

* For these experiments blood was withdrawn from the femoral vein. It seemed to us that the question of whether the oxygen content could be raised in this peripheral venous blood constituted a severer test than that provided by mixed venous blood from the right heart. We, of course, would have added such determinations had we not failed to get delay in the shock-time as a result of the high oxygen atmosphere, notwithstanding the great increase in the oxygen content of the femoral venous blood.

DISCUSSION —While it is true that most of the methods employed for producing experimental shock involve a complicated and confusing variety of traumatic stimuli in a single procedure, it is evident that the method of Seeley, Essex and Mann has this objection. The fact that clinical shock may be due to several simultaneous causes in a given patient, is no indication for needlessly complicating experimental procedures. Admittedly, the problem of how to produce experimental shock is a most difficult one, however, it can be pointed out that the intestinal manipulation method of producing traumatic shock involves at least four types of stimuli well known to lead to or aggravate the condition of shock. Tissue trauma, harmful nerve stimulation, chilling, plasma loss and dehydration. The last factor appears to be of major importance in the shock developed by this method. The multiplicity of these factors perhaps accounts for the variability of results obtained from one experiment to another, not only in our hands, but in the experiments reported by the originators of the method (cf. the large standard errors of the mean).

We have available the data of Seeley, Essex and Mann, and the confirmatory data of Kendrick⁸ (1939). These studies seem to have demonstrated that real delay in the onset of shock *under the special circumstances of this experiment* can be effected by barbiturates *in comparison with ether*. Our own data support this conclusion.

The major purpose of this communication, and the questions we wish to raise, are concerned primarily with the important assumptions that have been made by others concerning the implications of the work of Seeley, Essex and Mann. It has been assumed by numerous writers, on the basis of the report by Seeley, Essex and Mann, (although not by these men) that it is safe, and desirable, to recommend the use of barbiturates in wounded men with the aim of delaying shock, however it may be caused. Various references to bear this out could be given. More to the point in the present military situation is the official report of the Tenth International Congress of Military Medicine and Pharmacy held in Washington, D. C., May 7-15, 1939. On page 188, the statement is made that "*these experiments (of Seeley, Essex and Mann) indicate that patients to whom sodium amytal is administered early, more often survive the exposure, delay and transportation incident to their evacuation to installations of definitive treatment*" (Italics ours). This report goes on to say that "*with these facts in mind it seems advisable to equip battalion surgeons and collecting company personnel with sodium amytal—(to delay) the onset of shock*" The experiments under discussion may or may not be applicable to man subjected to the common types of shock producing trauma of the battle field.

Transference of the findings of Seeley, Essex and Mann, obtained from studies on anesthetized dogs to a general recommendation concerning the equipment of battalion surgeons and collecting company personnel for widespread application to seriously wounded soldiers, involves a good many assumptions. The interpreters of the Seeley, Essex and Mann data make at least two major suppositions that are difficult, if not impossible, to uphold

First, to have made the recommendations mentioned, it must have been assumed by the interpreters that the findings of Seeley, Essex and Mann (which they obtained in their specialized method of producing shock) hold for battle field shock in general, at least they must have supposed that the recommended barbiturate will not of itself constitute a real hazard. Evidence directly opposing both of these opinions is at hand. Second, use of the data obtained from the anesthetized dogs as a guide for treating wounded but unanesthetized men requires the assumption that the etherized dog represents unanesthetized man and that the dog under the influence of the barbiturate is comparable to man following the administration of barbiturates. In other words, it must be recognized by those who wish to transfer these findings to man that the data of Seeley, Essex and Mann do not compare an unanesthetized group of dogs with a group of dogs under a barbiturate. The comparison is between dogs under ether and dogs under a barbiturate. It would be a more accurate transference of the data in question if those who wish to apply these data to man would conclude that the wounded soldiers would be better off on receiving barbiturate than he would be if he received ether. Unfortunately, data are not available which permit the comparison of shocking stimuli with and without anesthesia, the available data merely present comparisons between the effects of one anesthetic agent and another. It seems apparent that recommendation of the general use of barbiturates for the prevention of shock in severely wounded soldiers, by battalion surgeons and collecting company personnel, is not securely founded, and there is considerable evidence that such use of the barbiturates may be dangerous.

While barbiturates delay the onset of shock in the intestine-manipulating experiments of Seeley, Essex and Mann, of Kendrick, and in ours, it must be recognized further that this is a special type of trauma, and all subjects are under anesthesia. As pointed out by Seeley, Essex and Mann, the method is probably effective chiefly through its dehydrating effect. The barbiturates appear to be more effective in preventing water and plasma loss from the exposed intestines than is ether. The chance that the difference between the two agents may appear simply because ether may increase this loss above normal or above that which is the case under barbiturates must be kept in mind. Seeley, Essex and Mann observed, as we have also, that the loss of fluid from the surface of the traumatized intestines was much less rapid under the barbiturates than under ether.

Other evidence could be cited to support the view that the plasma volume tends to be preserved or increased under the barbiturates whereas the reverse is true under ether. (Ref Hamlin and Gregeison⁶ (1939), McAllister⁹ (1938), Seales and Essex¹⁴ (1936), Adolph and Gerbas¹ (1933), Bourne, Bruger and Dwyer⁵ (1930), Barbour and Bourne² (1923) and others). Polderman and Beecher¹¹ (1942) have shown that the volume flow of cervical lymph is usually about 70 per cent greater under ether than under barbiturates. This adds one step to the probable explanation of the greater loss of fluid under ether and the more rapid decline in the

subject's condition under this agent than when under the barbiturates, under the special circumstances of this experiment

It must be emphasized, that if the barbiturates are effective only by virtue of their antidehydrating effects, then one could hardly expect them to be of value in shock due to other causes, as hemorrhage, tissue damage and so on, unless rapid fluid loss from large surfaces was a complicating factor. In these other types of shock it is reasonable to suppose that the barbiturates might be distinctly harmful, for their typical effects are undesirable—depression of the respiratory volume, decrease in, even loss of effectiveness of the normal respiratory stimulant, carbon dioxide (ref Beecher and Moyer³ (1941) for a discussion of this and references to other papers on the subject), depression of blood pressure, depression of the cardiac muscle, *etc*. These and many other effects of the barbiturates could be listed to emphasize that unless specifically indicated these agents had better be avoided in the seriously wounded.

SUMMARY AND CONCLUSIONS

1 We have confirmed the observation of Seeley, Essex and Mann that shock produced in dogs by exposure and manipulation of the intestines is slower to appear when barbiturate (sodium amytal) anesthesia is used than when ether anesthesia is employed.

2 No significant delay was found in the onset of shock produced by hemorrhage when barbiturate (sodium amytal) anesthesia was compared with ether anesthesia. This observation coupled with those of Parsons and Phemister, and Blalock, who found similar effects under barbiturate and ether anesthesia when shock was produced by muscle trauma, indicates that the barbiturates as compared with ether anesthesia are not useful in delaying all types of shock.

3 On the basis of the available evidence, the barbiturates appear to delay shock in comparison with ether, only when the chief shocking trauma is dehydration or plasma loss from wound surfaces.

4 Numerous recommendations have been made, on the basis of the work of Seeley, Essex and Mann (but not by these men), that barbiturates be administered to all wounded men if the development of shock is anticipated. Such recommendations involve two major assumptions, both of which, on the basis of the available information, are untenable. First, the numerous recommendations that barbiturates be administered routinely to all seriously wounded men involves the assumption that the barbiturates will be of value in shock, *however caused*, if one can judge by the results in dogs, this is not the case (see above), or at least the assumption is made that such administration of barbiturates will not be dangerous. Abundant evidence is available to indicate that this is not the case. Second, direct application as a shock preventive, of the observation mentioned in paragraph 1, above, requires the assumption that comparison of the barbiturate data with the ether data is the same thing as a comparison of barbiturate data with a condition of no anesthesia, certainly not the case. No data are available to indicate that the onset

of shock is slower under barbiturates than in unanesthetized subjects

5 In the experiments presented here, the administration of approximately 100% oxygen did not significantly delay, in comparison with room air, the onset of shock due to bleeding under either a barbiturate or ether, notwithstanding great elevation in peripheral venous blood oxygen content as a result of breathing the high oxygen atmosphere

REFERENCES

- ¹ Adolph, E F, and Geibasi, M J Blood Concentration Under the Influences of Amytal and Urethane *Am J Physiol*, **106**, 35-45, 1933
- ² Barbour, H G, and Bourne, W Heat Regulation and Water Exchange The Influence of Ether in Dogs *Am J Physiol*, **67**, 399-410, 1923
- ³ Beecher, H K, and Moyer, C A Mechanisms of Respiratory Failure Under Barbiturate Anesthesia (Evipal, Pentothal) *J Clin Investigation*, **20**, 549-566, 1941
- ⁴ Blalock, A A Comparison of the Effects of the Local Application of Heat and Cold in the Prevention and Treatment of Experimental Traumatic Shock *Surg*, **11**, 356-359, 1942
- ⁵ Bourne, W, Bruger, M, and Dreyer, N B The Effects of Sodium Amytal *Surg Gynec and Obst*, **51**, 356-360, 1930
- ⁶ Hamlin, E, and Gregerson, M I The Effect of Adrenaline, Nembutal and Sympathectomy on the Plasma Volume of the Cat *Am J Physiol*, **125**, 713-721, 1939
- ⁷ Hardenbergh, J G, and Mann, F C The Autoinhalation Method of Anesthesia in Canine Surgery *Jour Am Vet Med Assn*, **71**, 493-501, 1927
- ⁸ Kendrick, D B Results of Intravenous and Intra-arterial Administration of Fluids in Traumatic Shock Produced Experimentally *Surg*, **6**, 520-523, 1939
- ⁹ McAllister, F The Effect of Ether Anesthesia on the Volume of Plasma and Extracellular Fluid *Am J Physiol*, **124**, 391-397, 1938
- ¹⁰ Parsons, E, and Phemister, D B Hemorrhage and "Shock" in Traumatized Limbs *Surg Gynec and Obst*, **51**, 196-207, 1930
- ¹¹ Polderman, H, and Beecher, H K Unpublished data
- ¹² Rourke, M D, and Ernstene, A C A Method for Correcting the Erythrocyte Sedimentation Rate for Variations in the Cell Volume Percentage of Blood *J Clin Investigation*, **8**, 545-559, 1930
- ¹³ Sanford, A H, and Magath, T B A New Centrifuge Tube for Volume Index Determinations *J Lab and Clin Med*, **15**, 172-173, 1929
- ¹⁴ Searles, P W, and Essex, H E Changes in Blood in the Course of Ether Anesthesia and Sodium Amytal Anesthesia *Proc Staff Meet Mayo Clin*, **11**, 481-483, 1936 See also Searles, P W Effect of Ether and Sodium Amytal Anesthesia on Blood *Am J Surg*, **41**, 399-404, 1938
- ¹⁵ Seeley, S F, Essex, H E, and Mann, F C Comparative Studies on Traumatic Shock Under Ether and Under Sodium Amytal Anesthesia *ANNALS OF SURGERY*, **104**, 332-338, 1936
- ¹⁶ Shaw, J L, and Downing, V The Determination of Oxygen in Blood in the Presence of Ether by a Modification of the Van Slyke-Neill Technique *J Biol Chem*, **109**, 405-417, 1935
- ¹⁷ Snyder, J C The Cardiac Output and Oxygen Consumption of Nine Surgical Patients before and after Operation *J Clin Investigation*, **17**, 571-579, 1938
- ¹⁸ Tenth International Congress of Military Medicine and Pharmacy, Washington, D C, Official Reports I, 183-197, 1939 Practical Procedures for Anesthesia and Analgesia in War Surgery
- ¹⁹ Van Slyke, D D, and Neill, J M The Determination of Gases in Blood and other Solutions by Vacuum Extraction and Manometric Measurements *J Biol Chem*, **61**, 523-573, 1924

CHEST INJURIES*

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THE FOLLOWING was originally assembled to serve as a supplement to our colored moving picture "Chest Injuries" These films are to be used in connection with the instruction of Army medical officers However, in war time it is important for *all* physicians to be familiar not only with the clinical diagnosis of the various chest injuries, but also with the underlying pathologic physiology of the heart and lungs produced by these injuries With this knowledge the therapy will then seem simple and logical The immediate first-aid treatment to be administered at the site of the injury is presented first followed by the indications for, and technic of, the more specialized hospital procedures Finally we state the indications for surgery, the immediately corrective as well as those for the late sequelae Thus, in carrying the management of the patient from the place of injury through the specialized surgery that chest injuries entail, a practical compendium of thoracic trauma is presented Such an outline should be helpful to all physicians who are called upon to handle chest injuries as well as those who may eventually study the film

This material is presented in outline form, with the minimal amount of explanation possible The discussion is confined exclusively to the special therapeutic problems that arise in the management of chest wounds The treatment of shock and general care of the injured are not included

GENERAL PRINCIPLES

Impairment in the functions of the thoracic organs produces profound changes in the general physiology of the body Therefore, chest injuries demand immediate treatment, which differs widely from that employed in other regions At the outset, the problems are primarily those of mechanical derangement of the thoracic organs and hemorrhage, while later infection assumes a dominant role Certain general principles must be kept in mind in treating chest injuries

It is necessary

(1) To remove, widely and very gently, the clothing over the chest, so that exposure adequate for thorough examination may be obtained

(2) To promptly restore the normal relationship of the intrathoracic organs, which of themselves, may be largely responsible for shock

- a Cover open chest wounds
- b Control pneumothorax
- c Control cardiac tamponade

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- (3) To give immediate attention to shock and hemorrhage
- (4) To avoid movement of the injured until he can be transported to a place where hospital care may be administered
- (5) To watch constantly for the further accumulation of air or fluid in the pleural or pericardial cavities
- (6) To preserve the cough reflex by judicious sedation
- (7) To keep the bronchial tree free of blood and secretions
- (8) To support the chest wall where there is paradoxical or painful movement
- (9) To prevent or minimize sepsis—the direct or indirect cause of practically all late morbidity and mortality
- (10) To establish at once a reasonably high blood sulfonamide level, preferably sulfadiazine (8 to 10 mg per cent), by the administration of the sodium salt intravenously
- (11) To give precedence to the treatment of the chest wound in cases of multiple injuries of various parts of the body. Only the control of hemorrhage precedes the attention to the thoracic injury. However, in combined thoraco-abdominal wounds, every attempt must be made to improve the thoracic physiology so that abdominal exploration can be undertaken promptly
- (12) To employ, invariably, positive pressure anesthesia when open operations of the thorax are indicated

INJURIES REQUIRING CONSERVATIVE CARE

I THORACIC CONCUSSION (*Commotio Thoracis*)

Cause Nonpenetrating chest injury (exploding shells) produces a condition similar to cerebral concussion. Autopsies show no cause of death. Emotional strain and vasomotor reflexes are considered factors.

Signs and Symptoms Cold, clammy skin, slow, thready, irregular pulse, sighing respirations, unconsciousness.

Treatment As for shock (Oxygen of some value)

Prognosis If patients survive for a few minutes, they usually recover.

II TRAUMATIC ASPHYXIA

Cause Sudden, violent thoracic compression producing wave of back pressure, by way of the superior vena cava, dilating peripheral veins. This is followed by venous stasis and loss of vascular tone. Petechial hemorrhages frequent.

Signs and Symptoms Deep violet-blue discoloration of face and neck with edema, particularly of the eyelids and lips. Occasionally visual disturbances or permanent blindness. Skin dry and hot. Full bounding pulse. Stertorous respirations.

Treatment Morphine at once. Absolute rest. Head and shoulders to be somewhat elevated. (Oxygen may be of help.)

Prognosis If death does not supervene at once, recovery is probable.

III BLAST INJURY

Cause Impact on chest wall of wave of positive air pressure following bursting of a high explosive. There results, if the injury is a severe one, (1) multiple hemorrhages in the lungs, most pronounced along their anterior borders near the mediastinum, and (2) loss of pulmonary elastic recoil.

Signs and Symptoms Chest sometimes bulging. Normal percussion note but distant breath sounds. Bloody froth at mouth or nostrils. Shallow prolonged respiration, restlessness, prostration and grave shock. Surgical abdomen often simulated. Roentgenograms in conjunction with symptoms characteristic, scattered areas of patchy pneumonitis.

Treatment Morphine for restlessness, despite signs of asphyxia. Fowler's position to improve breathing. Oxygen but not artificial respiration. Intravenous fluids or whole blood transfusions *contraindicated*. Administer concentrated blood serum if necessary. Venesection frequently averts lung edema.

Prognosis Death may occur instantly. If one survives the first few hours, pulmonary edema developing, perhaps days later, may prove fatal. Therefore, it is important to minimize intravenous fluids.

FIRST-AID TREATMENT

At the moment the chest is injured, anxiety and restlessness develop. Cardiorespiratory embarrassment is shown by some degree of dyspnea and cyanosis. Often there is pain, seriously limiting respiration. Morphine in comparatively large doses should be administered at once. The patient should be kept warm. Elevation of the temperature above normal by excessive use of blankets or hot water bottles must be avoided, as peripheral vasodilation and loss of body fluids will result. These will add to the shock or throw a patient into shock if it is impending.

Unlike severe injuries elsewhere, the patient, if conscious, should be propped up to a semisitting position. He will then breathe more easily, and blood and mucus entering the bronchial tree may be promptly raised. If unconscious, he should be placed in the Trendelenberg position, so that blood and pharyngeal secretions will not be aspirated. If the dyspnea is the result of pain limiting inspiration, or if a crushing injury exists, after giving an adequate amount of morphine, adhesive strapping of the chest as described under "Stove-in Chest" may afford relief. Open sucking wounds of the thorax should be covered at once. Tension pneumothorax may be temporarily relieved by placing an open needle in the chest to prevent the accumulation of too much air. These conditions will be discussed later.

SURGICAL TREATMENT

The following emergencies, as encountered at the place where injury occurred, urgently require special and immediate attention.

I "SUCKING WOUND" OF CHEST WALL

Normally, during inspiration the ribs move outward and upward, the

sternum forward and upward, and the diaphragm downward. Thus the chest enlarges in all diameters. The volume of the lungs is proportionately increased by passively following the movements of the thoracic walls. The negative pressure thus created is at all times satisfied by the rush of air by way of the trachea, which is the only communication with the outside air.

When a chest wall injury extends through the parietal pleura into the pleural cavity (normally only a potential space), two openings are present to admit air into the thorax. While on inspiration air enters the chest through both of these openings, it is only by way of the trachea and bronchi that air, with its necessary oxygen, can reach the pulmonary alveoli. It is evident that the percentage of air that reaches the lungs through the trachea is in inverse proportion to the size of the chest wall opening. When this differential is sufficiently great, not enough oxygen is available to sustain life even with the deepest inspiratory effort. The prompt application of a reasonably air-tight dressing to close the chest wall opening averts this disaster.

On arrival at the hospital, the dressing applied to the sucking wound of the chest wall is removed. Débridement is painstakingly carried out, using a scalpel, not a scissors. A scissors squeezes as it divides, while a sharp scalpel cuts cleanly. A bit of muscle or fascia, whose nutritional future is hanging in the balance, might by this slight additional injury eventually become necrotic. The main purpose of this procedure is to excise all devitalized tissue.

The divided parietal pleura should be snugly closed if possible. However, this is rarely possible, so that the chest wall muscles or even the lung may be sutured across the pleural aperture. If this appears unsafe or impractical, one may be forced to resort to tight gauze packing as a temporary life-saving measure. Closed pleural drainage, using a thumb-sized tube, is then established as described under "Empyema—Closed Drainage."

After careful débridement and after the parietal pleura has been closed, all raw surfaces are sprinkled with 4-8 Gm of a sulfonamide. Because of the danger of infection no sutures are taken in the chest wall other than those necessary to close the pleura. The wound is then packed open with plain gauze. Rubber tissue applied directly over the open wound will prevent the gauze dressing from becoming adherent to the raw tissues (even vaselined gauze is painful to the patient on its removal). Powdering the wound twice daily with the sulfonamide is desirable. Healing time may be shortened by the application of adhesive strips upon the skin, to loosely approximate wound edges.

II TENSION (OR PRESSURE) PNEUMOTHORAX

A wound of the chest wall penetrating the parietal pleura, uncomplicated by injury to the lung, produces a pneumothorax. The closure of the chest wall opening, either by suture or dressing, effectually eliminates further

entrance of air. Subsequent aspiration of air before the injured arrives at the hospital is seldom necessary.

If, however, a laceration of the lung exists, complicating a penetrating wound of the chest, closure of the chest wall opening will remove but one source of the air accumulating between the lung and the chest wall. Bronchial branches torn open with the lung laceration allow air to escape through the torn visceral pleura with every inspiration. Almost always a check-valve mechanism at once occurs. That is, air enters the pleural space in inspiration by way of a bronchus in the lacerated lung, but in expiration it is impeded from escape because the lung tissues immediately surrounding the pleural opening are pressed together. Thus, a certain amount of air is retained. With each succeeding respiratory cycle the amount of imprisoned air increases. Air tension or pressure in the pleural cavity steadily increases. From the very moment of its inception, several important cardiorespiratory disturbances are initiated. The lung on the involved side is more and more collapsed. At the same time the mediastinum is pushed toward the opposite side at the expense of the contralateral lung, which, in turn, is steadily reduced in size. In the meantime, cardiovascular function, always intimately associated with respiratory disturbances, is becoming seriously affected. Unless relief is forthcoming, death supervenes. Immediate needle decompression, with or without syringe aspiration is life-saving.

Lung laceration with bronchial communication into the pleural space may occur following crushing injuries of the chest without any break in the continuity of the chest wall.

The diagnosis is not difficult. Dyspnea is of course the outstanding symptom. The side of chest containing the bronchopleural fistula is immobile. Percussion note is high. Breath sounds are absent.

Treatment Immediate introduction of a needle, preferably of large size. This should be left in place, anchored by adhesive straps, until patient arrives at hospital. The needle may be inserted in 2nd or 3rd interspace just lateral to midclavicular line.

Warning Do not needle indiscriminately left basal pneumothorax pockets as acute dilatation of the stomach or diaphragmatic herniation (discussed later) may be present.

On arrival at the hospital, if there are signs of accumulation of air in the affected pleural cavity, then the needle must be connected to an air-tight system under water, as depicted on the film. An air-tight intercostal catheter may be inserted into the pleural cavity and connected to a closed water bottle system in place of the needle. This has the advantage of allowing the escape of larger amounts of air and of offering less chance of trauma to the expanding lung, but has the disadvantage of presenting a greater chance of infection.

III CARDIAC TAMPONADE

Following injury to heart muscle or of intrapericardial vessels, hemorrhage into the pericardial sac may occur. As bleeding progresses, space for cardiac

action is steadily lessened. The auricles and vena cavae and finally the ventricles are compressed. The venous pressure rises. The arterial pressure falls. Inadequate oxygenation of circulating blood results. Serious tamponade of heart exists.

The diagnosis, when the possibility of its presence is considered, is not difficult, nor, fortunately, is the procedure for its temporary relief particularly complicated.

Duskiness of mucous membranes and nail beds or cyanosis is present, moderate shortness of breath, dyspnea or stertorous respirations, depending upon degree of tamponade, small thready pulse, low arterial pressure, high venous pressure, engorgement of veins of neck, sometimes venous pulsation. Cardiac pulsations are faint or absent over the pericardium. Cardiac dullness is not necessarily much increased.

There is usually a time-interval between the moment of actual injury and the onset of unconsciousness because of cardiac tamponade. The reason for this is found in the fact that it takes time for sufficient blood to leak out into the pericardium to actually tamponade the heart. As the tamponade becomes marked, the low arterial pressure and marked venous stasis result in serious interference with the oxygen supply to the brain.

If the imminent danger of immediate death does not contraindicate additional diagnostic measures, fluoroscopic examination will usually establish, with certainty, the diagnosis when the findings are considered in conjunction with the history, symptoms, and physical findings. One sees a cardiac shadow, but little larger than normal, with little or no evidence of pulsation.

Immediate aspiration of blood from the pericardium is imperative. The site of election is the left costoxiphoid angle. By this approach the needle not only avoids passing through both pleural leaves, but also cannot lead to injury of the lingula of the upper lobe of the lung were it adherent to the pleura in the precordial region. Furthermore, by this subcardiac approach the needle will enter the pericardium below the heart and not directly toward it, as would occur if aspiration was attempted through the chest wall. Finally, the pericardial sac can be more satisfactorily cleared of blood when aspiration is carried out from below.

After tissues are anesthetized with 1% novocain from the skin to pericardium, the aspirating needle (No. 15 gauge preferably) is inserted, directing it inward and slightly upward. The bevel on its distal end should be comparatively short. Usually the passage of the needle through the pericardium into the less resistant blood within the sac is easily appreciated as the needle advances. The larger the syringe attached to the needle, the less tactile sensation is retained. Since the pressure of the blood within the pericardial sac is positive, it is often advantageous to insert needle with no syringe at all, so that maximum appreciation of the resistance of the various structures (especially the pericardium) with which it progressively comes in contact may be recognized. Blood should escape at once when the pericardial sac has been entered. Then the syringe, with two-way valve, is at-

tached and all blood possible is aspirated under air-tight conditions. At all times during the procedure great care must be taken to avoid needle contact with heart muscle. The constant motion of the heart transmits along the needle, to the one who is aspirating, a scratching sensation. The needle must immediately be slightly withdrawn, for even superficial injury to heart muscle may result in prolonged oozing of blood from the cardiac abrasion, sufficient to produce tamponade in its own right, some time after needle has been withdrawn.

When the diagnosis is made before the patient has been taken to the hospital, aspiration should be accomplished immediately if patient is in serious condition and the needle and syringe are available. Even the withdrawal of 75 to 100 cc of blood may be temporarily life-saving. When, after thorough evacuation of the blood from the pericardial sac, signs of cardiac tamponade recur, surgical exploration for possible suture of the heart muscle or removal of foreign body is indicated.

The technic of intrapericardial exploration and suture of heart wound fall outside the scope of this discussion. It is shown in detail in the films on "Chest Injuries."

IV "STOVE-IN CHEST"

The injury consists of multiple rib fractures, often on two planes, anteriorly and laterally or anteriorly and posteriorly, usually limited to one hemithorax. The crushed side, because of its loss of rib support, cannot enlarge with inspiratory effort. The negative pressure created by the enlargement of the uninjured side of the chest in inspiration pulls the mediastinal organs toward the good side. The unoxygenated air in the lung of the injured side is actually sucked into the functioning one. In expiration both of these movements reverse. It follows then that the "stove-in" side of the chest actually decreases in size during inspiration, with a relative increase in size on expiration as the mediastinal organs return to midposition. The same air may move back and forth from the paradoxically moving lung to the good lung. The amount of air that goes back and forth between the lungs depends on the amount of paradoxical movement of the chest wall and the amount of mediastinal shift. This most inefficient type of respiration produces marked dyspnea. Severe pain on breathing that prevents even normal depth of inspiration may still further lessen oxygen supply.

Treatment (1) Give morphine in large enough doses to control pain, (2) strap chest with a completely encircling wide adhesive bandage at the level of the costal margin as described in the next paragraph, (3) aspirate retained secretions in the trachea by catheter or, if necessary, through bronchoscope, and (4) establish at once and maintain a high sulfonamide blood level to combat pneumonitis.

Adhesive placed at the costal margin level should completely encircle the chest when the diaphragm is involved, either directly or indirectly. If there exists contusion of the diaphragm, a diaphragmatic pleurisy or injury to the intercostal nerves whose anterior branches are in the vicinity of the

diaphragm, splinting of the affected diaphragm is desirable. The diaphragm however is a bilateral organ. In order to limit the excursion of either side, both must be splinted. An adhesive bandage completely encircling the chest is required, and proves of great benefit.

When adhesive so applied is not well supported, then it should be removed, replacing it with a tight adhesive band applied in expiration around the injured side of the chest. It should extend three inches onto the opposite hemithorax, both anteriorly and posteriorly.

Paradoxical motion of the chest wall may be greatly decreased by various mechanical contrivances. The Drinker respirator, or similar type, if available, is the best device, as it completely does away with the need for a firm chest wall until the ribs have knit sufficiently to offer strong support. If a respirator is not available, simpler measures may be employed. Several towel clips can be snapped through the soft tissue and under the ribs. On attaching the towel clips to a fixed overhead support, the depressed chest wall may be maintained in an elevated position.

V Hemothorax

The presence of a considerable amount of fluid between lung and chest wall produces characteristic signs, whether it be serous effusion, pus, or blood.

There is evident decrease in the mobility of the injured hemothorax. The degree depends upon the amount of blood present in the pleural space. The involved side often appears to be larger than the contralateral one. The percussion note is flat over the hemothorax. Tactile fremitus is absent. Breath sounds are usually absent. Pure bronchial breathing may be heard if the layer of blood is so thin that the breath sounds in the collapsed lung are transmitted through the blood to the chest wall.

When the lung is injured, in addition to the hemorrhage, air escapes from the bronchi. The presence of this air rising through the blood causes the percussion note to be tympanitic rather than flat. The signs then are predominately those of pneumothorax. The indications for relief in the field are those discussed under pneumothorax. On arrival at the hospital a roentgenogram will disclose the presence of the blood. If a film with the patient in the sitting position can be taken, without undue hazard, a fluid level establishes the diagnosis. If not advisable to raise the patient, a chest film with patient supine will show haziness—indicative of pleural fluid lateral to the lung, in a field that would be clear were air alone present.

First-aid treatment follows the general rules mentioned above—morphine, absolute rest, external heat. Aspiration of blood, except under rare circumstances, is contraindicated before arrival at the hospital. If death occurs during this period, it is usually from exsanguination, not from the pressure of extravasated blood against the mediastinum.

At the hospital, early aspiration of blood is desirable (24 hours after injury and before the 4th day).

Caution If an X-ray is not available, or the diaphragm has not been well visualized roentgenographically, before aspirating the left chest insert

the needle at the level of 5th or 6th intercostal space so as to avoid puncture of the diaphragm. Conceivably, the pressure of the blood against the injured lung has occluded the vessels responsible for the hemothorax. Premature reexpansion of the lung by the aspiration of the extravasated blood in the pleural space might cause bleeding to recur. To obviate this contingency, therefore, the blood aspirated during the first few hours after injury should be partially replaced with air. Blood removal appreciably shortens convalescence and permits the recognition of continued bleeding, also, whether or not the lung concealed by it is atelectatic. Extravasated blood produces extensive pleural irritation in some patients. Its early removal greatly reduces the danger of progressive pleural fibrosis. Furthermore, aspiration of the blood with partial replacement of air lessens the size of the pleural space should infection eventually develop.

If large clots are present in considerable amount, aspiration is not successful. It is frequently advisable to open the chest, remove clots, rinse out the pleural space with saline, sprinkle pleural surfaces liberally with a sulfonamide powder, and close the operative wound. The air remaining in the pleura after tight chest wall closure should be at once aspirated until a negative intrapleural pressure to five or ten centimeters of water be obtained. Higher pressures exerted on a lung resistant to sudden reexpansion because of thickened visceral pleura, may cause an outpouring of serum to satisfy the partial vacuum created by the aspiration of air. Subsequent removal of air in comparatively small amounts at daily intervals is the preferable procedure.

VI INFECTED HEMOTHORAX

Even when the blood in the pleural space is sterile, a daily temperature rise to 100°–101° F is usual. When, after several days there is an increase in temperature, pulse, and respiration, infection should be suspected.

The following findings point to an infected hemothorax: (1) Increased toxicity, (2) evidence that the amount of fluid in the pleural cavity is increasing (outpouring of serum from pleural irritation), and (3) the sample of blood aspirated has become purplish in color or has an unpleasant odor.

Bacteria often develop, at first only at some certain spot in the bloody fluid. So it may be several days before bacteria are prevalent throughout all the blood. The presence of purplish blood of unpleasant odor in an increasingly toxic patient is exceedingly suggestive, even though the culture of the blood aspirated is sterile. The complete and immediate removal of all the old blood, with adequate tube drainage of the pleural cavity (closed method) is highly desirable. The technic of pleural drainage is discussed elsewhere in the paper under "Empyema."

VII PENETRATING WOUNDS OF THE CHEST

The mortality rate following present day technic in intrathoracic operations is very low. In consequence, surgical exploration of intrathoracic injuries is much more frequent in the present war because

1 Foreign bodies can be removed. The presence of phosphorus in

incendiary bombs makes retention of even comparatively small bits of metal from them hazardous

2 In injuries both of the lung and chest wall, devitalized tissue can be débrided and the injury repaired. Openings in the lung may be closed in some cases

3 Bleeding vessels of the chest wall and lung can be ligated. Injury to the internal mammary and intercostal vessels may lead to serious intrapleural hemorrhage. Their ligation may be life-saving

4 Blood and clots between the pleural leaves or a superficial hematoma of the lung can be removed

5 The diaphragm can be examined as to evidence of injury to it. If an opening through the diaphragm is found, it is enlarged so that the intra-abdominal organs immediately below may be examined. By these procedures the danger of subsequent infection from bits of clothing, torn lung, *etc.*, may be greatly reduced, recovery hastened, and early or late death from hemorrhage, or sepsis averted

Before decision is made to explore, shock must be controlled. If possible, roentgenograms of the chest with patient in upright position to show fluid level, should be obtained. Air replacement of blood in the pleural cavity is of great diagnostic importance for reasons previously mentioned

VIII TRAUMATIC ATELECTASIS AND PNEUMONITIS

Cause The most important factor is the impairment in efficiency of the cough mechanism with the subsequent retention of bronchial secretions. It may be produced by the following conditions: (1) Voluntary splinting of the painful chest wall, (2) paradoxical movement of the chest wall, (3) oversedation, and (4) prolonged unconsciousness. Keeping the patient in one position causes hypoventilation of the lungs, while pulmonary hemorrhage may actually plug a bronchus and so directly cause atelectasis

Diagnosis The presence of retained secretions may be detected by finding coarse râles over the trachea and large bronchi. Cyanosis, fever, dyspnea progressing to coma, with concomitant chest signs, point towards an atelectasis or traumatic pneumonitis. There is usually dullness to percussion. Breath sounds, as a rule much decreased, vary from vesicular to bronchial. Râles are usually present over the affected area. The roentgenograms of the chest are diagnostic, showing changes varying from a scattered, patchy infiltration to a complete lobar haziness, with or without mediastinal shift, elevated diaphragm, or narrowed interspaces. Any fever in a patient with a chest injury should be considered as caused either by atelectasis or traumatic pneumonitis, unless proven otherwise

Treatment The prophylactic treatment is the more important. This includes supporting of the thoracic wall by adhesive taping and the use of shot-bags, and encouraging the patient to cough by the manual holding of the chest wall, which lessens the chest pain. Enough morphine should be used so that pain does not prevent the patient from coughing. Over-

doses of opiates or barbiturates that result in long periods of coma or semi-stupor, when the patient cannot cough voluntarily, are to be studiously avoided. Ten per cent carbon dioxide (not carbogen) is an important aid. The patient should be turned from side-to-side every two hours if possible, and expectorants and inhalants utilized to make the sputum less tenacious and hence more easily raised. A high blood sulfonamide level should be established early in all cases of chest trauma where injury has been severe enough to produce atelectasis or traumatic pneumonitis.

Catheter suction of the trachea and bronchi is, in most instances, the procedure of choice, to aspirate retained secretions and blood. The convenient technic is that of inserting a No. 16 urethral catheter through the nares and advancing it through the larynx on deep inspiration. The simplicity of this method is shown on the film, and can be mastered after a little practice. Local anesthesia produced by spraying the throat with two per cent pontocaine, will facilitate the passage of the catheter into the larynx, especially in the presence of an active gag reflex. Similarly, spraying the nasal mucosa with pontocaine lessens the discomfort to the patient. There is no contraindication of local anesthesia to the throat if fluids by mouth are withheld until the gag reflex returns (two hours). The catheter is attached to an ordinary "nose and throat" type of suction device capable of producing 15 pounds of pressure. The catheter may then be advanced down the trachea. By turning the head to the right side, the catheter may be introduced into the left main bronchus, and by turning the head to the left side, after withdrawing the catheter a little, it may be introduced into the right main bronchus. The suction should be applied intermittently so that too much air is not completely drawn out of the bronchial tree at one time. Cough is stimulated by the irritation of the catheter on the tracheal and bronchial mucosa so that frequently more sputum is coughed up around the catheter than is aspirated through it. This procedure has the advantage of being readily available, of being simple, and may be quickly set up and instituted, and used repeatedly on one patient. We believe too little attention throughout the country has been paid to this simple and highly efficacious procedure.

Bronchoscopy, of course, is more thorough, and should be employed when it is impossible to pass the catheter or where a thick mucous plug or blood clot resists removal by the catheter. It should be undertaken in preference to catheter suction where foreign body is a possibility or vomitus has been aspirated. The trained bronchoscopist can easily perform this procedure (as shown on the film) without moving the patient from his bed. The fact that the patient is critically ill is not a contraindication to bronchoscopy when atelectasis is present, as this condition may be the principal cause of the precarious state of the patient. Bronchoscopy in bed causes no more serious disturbance to the patient than that resultant from hard coughing, a respiratory exercise that usually is most desirable.

IX SUBCUTANEOUS EMPHYSEMA

Following chest injuries both penetrating and nonpenetrating, bronchial communication may occur between torn lung and subcutaneous tissues

Swelling and crepitation beneath the skin indicate the site of subcutaneous air. While gas-forming bacteria may be responsible for the presence of air beneath the skin, the absence of toxic symptoms, of edema, and of dark red or coppery discoloration of skin, render the latter source of the crepitations untenable. If emphysema is steadily progressive until most, or all, of the body is involved, open operation near the site of injury to repair the injured lung and close the open bronchus may be indicated. It is seldom, however, that such operative measures become necessary.

X MEDIASTINAL EMPHYSEMA

Cause Rupture of bronchus in or near mediastinum, rupture of bronchus deep in the lung with extension of air along the peribronchial tissues

Symptoms Subcutaneous emphysema first appears in episternal notch but may spread extensively under skin of head, trunk and extremities. There may be dysphagia, dyspnea, cyanosis, pneumatic extrapericardial tamponade, distension of the neck veins, and finally circulatory failure.

Treatment Palliative transverse incision at jugulum through platysma. By blunt dissection with finger, opening may be extended beneath manubrium into mediastinum.

Curative Attack surgically at source if condition of the patient is critical.

XI MISCELLANEOUS

Acute dilatation of the stomach occasionally occurs at a most serious complication of crushing injuries of the chest, with or without phrenic nerve paralysis on the left. Vomiting, when present, especially if accompanied by distention or tympany over the upper abdomen, is highly suggestive. A left basal pneumothorax may be simulated. Even though these findings are present only in a slight degree, acute dilatation of the stomach must be suspected when the patient, becoming steadily worse, has a rising pulse and a falling temperature. The passing of a stomach tube, an extremely simple procedure, is life-saving.

Rupture of the diaphragm, with the herniation of the abdominal contents up into the chest cavity, may produce dramatic and alarming symptoms. Extreme dyspnea, vomiting, with the signs of fluid and air in the lower left chest may be present. Borborygmus, if demonstrable, is diagnostic. Needling of left lower chest must be postponed until diaphragmatic dome has been visualized roentgenographically. If the diaphragm cannot be identified on the plain film and barium is not available, the giving of soda bicarbonate by mouth, followed by a few drops of dilute hydrochloric acid will produce a gas bubble to readily identify the diaphragm.

The surgical repair of the diaphragmatic herniation should be postponed if possible until the patient has otherwise made a complete convalescence.

INFECTIONS OF THE THORACIC ORGANS FOLLOWING TRAUMA

With prompt débridement of open chest wounds, the use of the sulfonamides, and attention to the principles outlined earlier in this paper, many thoracic infections following trauma can be prevented. However, because of the exigencies of modern warfare it is often impossible for a large number of cases to receive adequate early first-aid or hospital treatment. If these cases survive the initial shock and hemorrhage, infection of the chest organs will be a common finding. In some cases, too, in spite of the most painstaking early care, infection will ensue. Therefore, no summary of the management of chest injuries is complete without a brief discussion of the common infections of the thoracic organs that follow trauma.

I INFECTIONS OF SOFT TISSUES OF CHEST WALL

Infections of the soft tissues of the chest wall differ little from those elsewhere in the body, with one outstanding exception. The chest wall may become infected by anaerobic organisms from a putrid empyema or lung abscess, either through a needle track or direct extension of the inflammatory process. In either case a fulminating cellulitis develops that is often rapidly fatal. Prophylactically, the prompt institution of surgical drainage of the putrid empyema will avoid multiple and hazardous needlings through the chest wall.

The usual procedure, in the attempt to control a rapidly progressive cellulitis of the chest wall, has been to make long parallel incisions through to the floor of these infected areas, extending the incisions well into apparently uninvolved tissue on either side. The wound edges are widely undermined with the fingers and rubber drains inserted plentifully to hold the infected surfaces apart. Uniformly, these patients at operation are profoundly toxic. The surgeon, by the above method, frequently administers the *coup-de-grace* by ruthlessly breaking down whatever barriers the body has been able to erect against the invading bacteria.

We have found it much more satisfactory to make a wide incision in the uninfected tissue across the path of the oncoming bacterial invasion, an inch or more in front of the infected area. Usually the spread is extending in but two directions. Two such incisions should be all that would be required to halt this process. Vaseline gauze is placed in these zonal incisions to prevent, temporarily, apposition of the wound edges. As a rule, limitation of the infection is thus established. After these incisions peripheral to the spreading cellulitis are completed, one or perhaps two cuts are very gently carried through into the infected planes, avoiding any molestation of the surrounding tissues. Liquefaction, which usually occurs within a day or two, is easily controlled by multiple small incisions, with minimal danger of disturbance to surrounding tissues. Subpectoral and subscapular abscesses may be the source of occult fever during their early stages. Sooner or later local pain, tenderness, swelling, and fluctuation will point to the diagnosis. Wide drainage with the dependent placing of multiple rubber-dam drains

generally is effectual in draining these abscesses. If they persist over a period of time, one must be on guard for a possible osteomyelitis of an adjacent bone.

II OSTEOMYELITIS OF RIBS AND STERNUM

Osteomyelitis of the ribs practically always follows trauma and is rarely a part of osteomyelitis with multiple involvement of other bones of the skeleton. Simple fractures of the ribs are practically never complicated by osteomyelitis. However, osteomyelitis of the ribs does occur in infected compound fractures and when chest wall infections and empyema are present, if any bare rib deprived of its nourishing periosteum is exposed in the infected wound.

Diagnosis The diagnosis is made by the history of local trauma, the signs of a low grade infection, and local tenderness. Roentgenologic examination almost always shows the erosion and periosteal proliferation typical of osteomyelitis.

Treatment The treatment consists of wide excision of the involved bone down to healthy osseous tissue. If a cartilage is exposed, or infected it must be completely removed, otherwise permanent healing will not take place.

In a similar manner osteomyelitis of the sternum usually follows trauma. More constitutional reaction is present and there is local tenderness, swelling and redness. Although it is sometimes difficult to demonstrate the lesion, the roentgenograms show typical signs of osteomyelitis. Because the complications of retrosternal abscess and anterior mediastinitis are serious, wide excision of the involved bone and adjacent costal cartilages is indicated.

III EMPYEMA

Empyema is the most common thoracic infection following chest injuries. This is true because of the high frequency of cases in which the pleura is soiled by penetrating wounds and because empyema is not an uncommon complication of pneumonia and lung abscess.

Diagnosis Empyema that follows thoracic trauma is usually not difficult to diagnose. If there has been a penetrating wound, usually débridement and drainage has not been adequately carried out. There is a high septic-type of fever with corresponding elevation of pulse and rapid respiration. The physical signs are those of fluid, which often accumulates very rapidly. The roentgenogram shows signs of pleural fluid on the involved side. In the absence of gas-forming organisms, no fluid level will be seen unless there has been a tear of the lung or an open pyopneumothorax is present. The diagnosis is made by the aspiration of purulent fluid from the pleural cavity. Immediate smear and culture of the pleural fluid must be done, as often it is impossible to demonstrate the organisms after the material has stood overnight. Before drainage is undertaken, unless the odor of the pus is foul, pyogenic organisms must be demonstrated in the pleural fluid.

TREATMENT

1 *Open Drainage* Open drainage with rib resection, under local anesthesia, and the insertion of a large tube is the procedure of choice. However,

certain conditions must obtain. In the discussion on "Sucking Wound of Chest Wall," the dangers of the open pneumothorax were emphasized. When the pus aspirated from the pleural cavity is thin, there is little fibrin content and, therefore, few adhesions are present along the mediastinal pleura. Hence, the mediastinum is mobile. Drainage at this time would subject the patient to the dangers of the open pneumothorax and possible fatal issue. Therefore, needle aspiration is the preferred treatment early in acute pyogenic empyema, not only so that the mediastinum will be fixed, but also that the size of the empyema pocket shall be limited. When the fluid contains 80-90 per cent sediment, open drainage with rib resection and the dependent placing of a thumb-sized tube, large enough to evacuate thick pus and fibrin, is the procedure of choice. If a pyopneumothorax is not present, 50-100 cc of the pus aspirated may be safely replaced with air to produce a fluid level. Then with a lateral decubitus roentgenogram the bottom of the pleural pocket may be accurately determined. However, if such a roentgenogram is not available, it is safe to resect the rib immediately above the lowest intercostal space where pus was obtained by aspiration. We do not completely aspirate all the pus from the pleural cavity immediately before surgery, as it may be impossible to find the pocket in the operating room.

2 *Closed Drainage (Large Tube)* Because the lumen of an intercostal catheter is not large enough to permit the drainage of thick pus, fibrin, and blood clots, we feel that it is not indicated in empyema. We reserve this method (1) to drain uninfected bloody serum in clean operations, and (2) to allow the escape of air in tension pneumothorax, where the needle method of reduction of air pressure has not been successful. To effect closed drainage with a large tube, a six-centimeter segment of rib is resected, under local anesthesia, at the posterior axillary line. Providing the resultant drainage is dependent, this site is desirable as the patient does not have to lie on the tube. The bottom of the pleural pocket is determined according to the technic described under "Open Drainage of Empyema." Through an opening in the parietal pleura, just large enough to admit it, a thumb-sized tube is snugly inserted into the pleural cavity. This tube is then connected to a drainage bottle on the floor with an underwater seal. The soft tissues overlying the parietal pleura are not sutured but approximated by flamed adhesive strips applied to the skin. Thus, the air-tight closure is helped by this strapping, and yet infected secretions are not dammed up in the soft tissues. By using this method (depicted on the film) air-tight drainage is maintained, yet the use of a thumb-sized tube permits the drainage of thick pus and fibrin. This type of drainage following chest injuries is indicated in

a *Chest Injuries where Pleura is Grossly Contaminated* Here, following debridement, because the mediastinum is not fixed, closed drainage is indicated. (The use of a large tube makes it adequate)

b *Open Operations of the Thoracic Cavity where the Pleura is Grossly Contaminated—such as Lobectomy* The tube in this case should be put in posteriorly to drain the hilum

c *Putrid Empyema*, if caused by a highly virulent strain of organism, should be drained early, because repeated aspirations lead to phlegmon of the chest wall. Since the mediastinum is not fixed *early*, closed drainage is necessary.

d *Chronic Empyema—where Highly Negative Suction Therapy is Indicated*. Prompt, adequate drainage usually prevents the acute empyema from becoming chronic. However, if the drainage tube is too high, too small, or pulled out before the pleural space is obliterated, chronicity may result. The presence of foreign bodies, bronchopleural fistulae, tuberculosis, fungi, or osteomyelitis of the ribs, may also make the empyema chronic.

The Schede thoracoplasty is the time-honored treatment for this condition. Recently we have used marked negative intrapleural suction through the use of a large drainage tube. Although it is not always successful, it should be tried before the Schede thoracoplasty.

IV LUNG ABSCESS

Lung abscess may follow penetrating or nonpenetrating wounds of the chest. When the patient is unconscious from shock on the battlefield, the aspiration of secretions from the upper respiratory track (particularly if oral sepsis is present) may be followed by pulmonary abscess. Bronchial obstruction caused by the aspiration of a foreign body or clots from pulmonary hemorrhage and less often septic emboli may also cause pulmonary abscess following injury to the chest.

Diagnosis. The diagnosis of lung abscess in a patient with a severe thoracic injury may be difficult, as other conditions may mask symptoms referable to the abscess. Chills and high temperature occur first, followed by a harassing dry cough that soon is productive of blood-streaked mucus. The raising of foul gas precedes the "vomica" or sudden coughing up of profuse amounts of purulent or foul sputum as the abscess breaks into the bronchus. Foul sputum is the most important diagnostic sign as it almost invariably means pulmonary destruction. Putrid bronchiectasis and the rupture of a putrid empyema into a bronchus are the two other main conditions resulting in foul sputum. The physical findings are notoriously deceptive. Rarely are the physical signs of cavity present in acute lung abscess. Dullness, diminished breath sounds, and medium to coarse râles are common findings. The roentgenogram is usually diagnostic, showing, at first, an area of dense "infiltration" and then a cavity with a fluid level. However, as long as the draining bronchus is blocked and the lung abscess cavity completely full, no fluid level can be seen. Care must be employed to take the roentgenogram in the upright position (to demonstrate a fluid level) just after the patient has raised considerable amounts of sputum, so that the level may be present.

Treatment. As soon as the diagnosis of lung abscess is made, medical measures should be at once instituted. In addition to sulfonamide therapy and a good hygienic regimen, indicated for all pyogenic infections, postural drainage (if with change of position cough not alarmingly violent) and bron-

choscopy are of first importance. The branch bronchus draining a lung abscess is always severely inflamed—leading to obstruction of this bronchus because of the edema and swelling of the mucosa. At bronchoscopy, shrinking solutions can be directly applied to the swollen mucosa. The pus may thus be aspirated as the drainage into the main bronchus is improved. Frequently during the first hours following bronchoscopy, expectoration of pus is particularly copious. Therefore, bronchoscopy, should be uniformly employed in pulmonary abscess. Because there exists a constant chance of spread of the infection to other lobes and because the lung abscess walls become fibrous after a time, the sooner the bronchoscopy is done the better. The clinical course, as shown by fever, toxicity, and amount of sputum, is important in evaluating the progress of the patient. However, the chest roentgenogram is the deciding factor. If the roentgenogram shows no *definite* diminution in the size of the abscess cavity after bronchoscopy, in spite of apparent clinical improvement, external drainage is indicated. It is a prevalent medical opinion that after the diagnosis of lung abscess is made, one to two months should elapse to allow the patient to heal spontaneously. With the present day technic of surgical drainage under local anesthesia, as shown on the authors' films dealing with "Chest Injuries," the percentage of cures is so high, and the mortality so low, that this unnecessary delay is unwarranted. Time does not permit us to cite the evidence for external drainage. Yet our results of early surgical drainage have been so good that we can categorically state, that when a lung abscess stops improving and becomes stationary in its course, constant danger of spread exists and drainage is at once indicated.

The postoperative care is important and entails constant vigilance to make sure that the pulmonary pocket is healed before the chest wall sinus is allowed to close. Because of success in closing the pulmonary pockets with fat grafts (technic illustrated on film), we are using them almost as a routine measure to shorten the otherwise often prolonged convalescence of the patient.

V SUPPURATIVE PERICARDITIS

Diagnosis Suppurative pericarditis follows penetrating wounds and foreign bodies of the pericardium. It is also secondary to pneumonia and empyema. In addition to the general signs of marked sepsis, enlarged precordial dullness, the signs of cardiac tamponade described earlier, and a palpable tender liver are present. The heart shadow is diffusely widened at the apex and base. Aspiration of purulent material by a needle in the costophrenoid angle, as depicted on the film, is necessary to make the diagnosis.

Treatment The treatment consists of general supportive measures, sulfonamides intrapericardially, and surgical drainage as soon as pyogenic organisms are demonstrated in the pericardial fluid on smear or culture. A parasternal incision, with resection of the entire 5th cartilage, or an incision parallel with and beneath the costal margin may adequately drain the pericardium without opening the pleural or peritoneal cavities.

VI MEDIASTINITIS

Diagnosis Rupture of the esophagus or trachea, whether from actual

perforation or due to a nonpenetrating wound, is the most common cause of mediastinitis accompanying thoracic trauma. Infected foreign bodies in the mediastinal tissues present another important cause of acute mediastinitis in persons with chest injuries. The breakdown of suppurative mediastinal lymph nodes or the spread of infections from adjacent organs also results in mediastinitis. The pus which is located in either the anterior or posterior mediastinum, may break out through the intercostal spaces or follow the fascial planes to the neck or extend downward between the pillars of the diaphragm.

The signs and symptoms are those of a fulminating inflammatory process plus the effect of pressure on the mediastinal structures. Frequently the general constitutional reaction is so severe as to mask the focal symptoms. Infection in the anterior mediastinum results in pain under the sternum, dilatation of superficial veins, dyspnea, respiratory stridor, tenderness on pressure on the sternum. If the posterior mediastinum is involved, pain between the shoulder blades, dysphagia, dyspnea occur. Dullness in the paravertebral region or increased anterior mediastinal dullness may be present. The roentgenogram generally shows a widening of the anterior or posterior mediastinal shadows. Air may be present. A fluid level helps in the localization especially if, lateral, oblique, and decubitus films are taken.

Treatment In addition to general supportive measures and sulfonamide therapy, the treatment consists of early surgical drainage. If the abscess is in the anterior mediastinum, a paramediastinal incision is made, with complete removal of the incised cartilage to prevent certain chondritis of the remaining stump. The pleural space is avoided and the mediastinal pocket entered. If a posterior mediastinal abscess is above the fourth rib, it may be drained in the cervical region, entering at the anterior margin of the sternocleidomastoid muscle. Below the level of the fourth rib, resection of mesial segments of two or three ribs along with their corresponding transverse processes at the appropriate level, will lead to the exposure of the abscess cavity. The pleura is retracted laterally and soft rubber tubes, rubber dam, or gauze is inserted. Since the mortality without surgery is 80 per cent, and that with surgery is 30 per cent, early operation is recommended for this desperate condition.

VII BRONCHIECTASIS

Bronchiectasis is such a late sequela of thoracic trauma that it is inserted here only for completeness, and warrants only the briefest remarks. Bronchiectasis follows a long-standing obstruction of the bronchus such as an undetected foreign body in the bronchus. It is also a complication of chronic lung abscess and suppurative pneumonitis. If the infections discussed earlier in the article are promptly and thoroughly dealt with, few cases, indeed, will end up with bronchiectasis. When any of these cases discussed above drag out, with chronic cough and expectoration, or repeated hemoptysis, bronchiectasis should be suspected.

The diagnosis is made only by outlining the bronchial tree with lipiodol dropped into the trachea. Bronchoscopy, however, should be always performed to rule out foreign body, granuloma, or tumor. Palliative measures

such as postural drainage and repeated bronchoscopies are of some benefit. If the bronchiectasis is sufficiently localized, lobectomy and pneumonectomy (as shown on the film) are curative.

SUMMARY

Approximately 25 per cent of the patients with thoracic injuries die between the field and the collecting station. The treatment of chest injuries should, therefore, take precedence over those of other parts of the body. An exception is the control of hemorrhage. Since shock may be directly due to serious cardiorespiratory disturbances it is often of vital importance that the chest emergency be cared for first. The cause removed or alleviated, shock may cease to be of moment. A thorough knowledge of the signs and symptoms, previously explained in this discussion, particularly those of cardiorespiratory disturbance, is, therefore, necessary. Once the diagnosis is established the immediate and perhaps urgently required treatment is as a rule comparatively simple.

- 1 The Closure of a Sucking Wound of the Chest Wall
- 2 The Aspiration of Air to Relieve a Pressure Pneumothorax
- 3 The Aspiration of a Cardiac Tamponade

Even upon arrival at the hospital, open operations into the chest are not to be lightly undertaken. In the most skilled hands great, and sometimes disastrous, complications may be encountered. If there appears no clear purpose for surgical exploration it is wise not to explore until some definite indication does present itself. It is particularly important that the anesthetist be trained in tracheal intubation, and that adequate facilities are provided for positive pressure anesthesia. Seldom, indeed, is there justification in attempting a procedure of any magnitude before the injured has reached a hospital.

"Reparative Surgery" that can be postponed without undue hazard should be delayed until the condition of the patient has improved sufficiently to permit it. Infection must be fought by the prompt establishment of a high sulfonamide blood level and by early surgical drainage following the principles discussed in this paper.

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PILONIDAL CYSTS AND SINUSES A METHOD OF WOUND CLOSURE*

REVIEW OF 230 CASES

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A PILONIDAL SINUS OR CYST, known in the European literature as a sacrococcygeal sinus or cyst, is ordinarily thought of as a minor ailment and few clinics have devoted any particular care or study to the disease. As a rule its operative treatment and after-care are left to the less experienced members of the surgical staff who understand thoroughly the need of complete eradication, but often do not appreciate the importance of the subsequent treatment of the wound. With the best of care, the postoperative wound may require weeks and even months to heal. From the civilian point of view the time of actual disability is not long, but the extended period of dressings is a nuisance to the patient and to his physician. In the Army, on the other hand, a soldier must remain in the hospital until the wound is completely healed and he is able to return to full duty. This is often a matter of several weeks, or even months, and during this time not only the soldier's services are lost but he also becomes a liability to his government. A shortening of the healing period, therefore, is obviously desirable.

Recognition is usually given to Jonathan M. Warren,¹ of Boston, as the first to have called attention to this disease. In 1854, he described an "Abscess Containing Hair on the Nates," which undoubtedly was an infected pilonidal sinus. In 1867, he² reported further experiences with the condition and gave an excellent clinical description of the disease as we know it today. Credit for the first report of a case, however, apparently should go to A. W. Anderson,³ also of Boston, who, in 1847, told of having extracted hair from an ulcer in the sacrococcygeal region.

As the disease became better known, considerable speculation naturally arose as to its etiology. There have been two principal theories concerning its origin, both of which concede its congenital nature.

One theory explains these epithelial sinuses and cysts as being derived from imperfect involution of the epithelial cells that participate in the formation of the embryonal medullary canal and its surrounding medullary, or neural, tube. Normally the caudal portion of the medullary canal and tube become almost completely obliterated during intra-uterine life and are represented at birth by the filum terminale which extends from the distal end of the spinal cord to the back of the first segment of the coccyx^{4, 5}. It is conceived that epithelial cells of the caudal end of the neural tube may sometimes persist to adult life and, as epithelial rests, give rise to

* Read before the Fort Devens Society of Medical Department Officers, May 19, 1942

pilonidal sinuses and cysts This theory was advanced by Tourneau and Herrmann,⁶ in 1887, and has received considerable support, notably from Mallory,⁷ and Gage⁸ Further evidence tending to confirm a developmental relationship between pilonidal sinus and the cord is afforded by Moise,⁹ and by Ripley and Thompson,¹⁰ who reported cases in which sinuses in the sacrococcygeal region became the route of infection for meningitis

According to a second theory, pilonidal sinuses and cysts are derived from the skin through a process of invagination, which takes place during intra-uterine life In describing the case of a young girl with multiple congenital anomalies Féré¹¹ referred to what appears to have been a pilonidal sinus as a cutaneous infundibulum of the saciococcygeal region Stone¹² apparently accepted the theory of cutaneous invagination but was at a loss to explain why this inversion takes place He¹³ later conceived the idea that this development in the human was comparable to the invagination of skin structures seen in the preen gland of birds and represented an atavistic tendency in man Fox,¹⁴ basing his opinion on embryologic studies, was thoroughly convinced that pilonidal sinus is a derivation of skin ectoderm and not neurogenic or enteric in origin Kooistra,¹⁵ after sectioning a number of embryos, found evidence to support both theories, and the matter still remains unsettled

There is some indication that heredity may be a factor, though probably a small one, in the occurrence of pilonidal sinuses Cases are sometimes found in more than one member of a family, and their presence in identical twins has been reported by Mechling,¹⁶ and by Goldberg and Bloomenthal¹⁷ The disease is occasionally associated with other congenital anomalies, as in the case reported by Feré,¹¹ but this is by no means the rule In most of the large series reported there are one or more instances of spina bifida, but this probably is incidental

Pilonidal sinuses are preponderantly a disease of young adult males and, therefore, become a matter of some military importance at this time The ratio of males to females is usually reported as something like three or four to one In the series to be herein reported the ratio is approximately three males to one female Newell,¹⁸ however, reported a predominance in the female Some idea of the general incidence of the disease may be obtained from Kooistra's¹⁵ finding that a diagnosis of pilonidal sinus was made on 350 of 313,285 patients admitted to the University Hospital, Ann Arbor, during a period of 14 years, an incidence of approximately 1/940 Seventeen of the 350 were recurrent lesions As a rule the sinus or cyst gives no trouble before puberty Attempts have been made to directly relate the onset of symptoms to the development of the sex glands, but there appears to be little evidence to support this thesis It is probable that the development of hair which occurs at this period has something to do with the production of irritation in the sinus, but this assumption is open to question because not all pilonidal sinuses are hair-bearing In Kooistra's¹⁵ series 52 per cent contained hair, and in the cases reported by Smith¹⁹ hair was found in only 40 per cent

The disease appears to belong almost exclusively to the white race. A few cases in the Negro have been reported but Kooistra¹⁵ states that no cases have been reported in the yellow, brown, and red races. The people of these races have relatively little hair on the body and this may be one factor in the absence of pilonidal sinus disease. Our series of 214 patients is made up of 55 Italians, 47 Central Europeans, 41 Jews, 24 Anglo-Americans, 16 Irish, 8 Poles, 5 Greeks, 5 Russians, 3 Armenians, 2 Negroes, 1 Spaniard, 1 Maltese, 1 Finn, 1 Turk, and 4 of undetermined origin. Considering the mixed population of the City of New York the racial distribution of cases is probably of small statistical value.

There is some difference of opinion as to the importance of trauma in the activation of a pilonidal sinus. Thirty-two per cent of Kooistra's¹⁵ 350 cases gave a definite history of injury, but 87 per cent gave no history of injury within a month of the onset of symptoms. Of our 214 patients, only 13, or 6 per cent, attributed the onset to direct injury. In addition to this number it is interesting that five of the 57 female patients in the series, or 8.8 per cent, gave childbirth as the cause of onset and two others stated that symptoms began during pregnancy. Kooistra¹⁵ was of the opinion that injury is a relatively unimportant factor in the etiology of pilonidal sinus, and in this he is supported by Biedenbach and Wilson,²⁰ and others. In military surgery, however, one is impressed by the number of cases coming from the mechanized units where scant cushioning of metal seats is the rule.

Fundamentally, the lesion consists of a single sinus or of multiple midline sinuses leading to one or more cystic cavities situated in the subcutaneous fatty and fibrous tissue overlying the region of the lower sacrum and coccyx. The external opening is situated caudal to the cyst and a probe entering it passes obliquely in an anterior and cephalic direction. According to Rogers,²¹ 70 per cent of the sinus tracts are of this simple variety. He found no evidence that the epithelial rests constituting the original congenital defect had any tendency to extend except as they were forcibly displaced by abscess and scar tissue formation. David²² is also of the opinion that the complications of epithelial arrangement are caused by the development of an abscess within the cyst which upon rupturing into the surrounding tissues carries with it a part of the cyst wall. The displaced portion of cyst wall gradually forms a new cavity lined with epithelium. Whatever the explanation may be, it is well known that some of the tracts do have ramifications.

The great majority of cases have some degree of infection and, as a rule, there is a history of abscess or of drainage from the sinus. Infection was present in all of Roger's²¹ cases. The same was true of virtually all of the 214 patients comprising the series being reported. Exactly one-half of the 214 gave a history of one or more abscesses which had either been incised or had ruptured spontaneously.

The symptoms and signs of the disease are too well known to warrant extended discussion. They are due almost entirely to the infection, which

differs clinically from ordinary infections by persisting for a long time after drainage has been established. The infection rarely gives rise to a bacteremia, but in one of our cases arthritic symptoms appeared to be definitely related to exacerbations of the infection in the sinus.

Differentiation of this disease from other conditions which manifest themselves in the same region is usually not difficult. Occasionally the opening of a sinus near the tip of the coccyx is mistaken for an anal fistula, but the careful introduction of a probe or a roentgenogram following the injection of radiopaque medium will as a rule establish the diagnosis. An infected sinus or cyst may be mistaken for an ordinary abscess but this is no longer a common error.

The treatment consists essentially in the removal or destruction of the tissues that make up the sinus or cyst, particularly the epithelial elements, but there is some difference of opinion as to how this is most satisfactorily accomplished. There are two general methods, one is a direct attack on the sinus itself, the other attempts to encompass and remove the tissues which contain the sinus. Either method is effective if properly applied, but recurrence or persistence has been and continues to be a problem, and the time required for healing is often long.

Direct attack upon the sinus is usually made with a destructive chemical or the cautery. Anderson,³ who reported the first case of pilonidal sinus in 1847, opened the mouth of the sinus and used injections of silver nitrate and chloride of mercury without any perceptible benefit. He then made an opening in the cavity and three weeks later found the patient entirely well. The chemical treatment of pilonidal sinuses has not been widely adopted since this first trial, but with improved solutions and better technic more favorable results have been obtained, and the method has gained a certain number of adherents^{23, 24, 25}. Rogers,^{21, 26, 27, 28} and his associates, have been consistent advocates of cautery excision and this method, in their hands, has given very good results, particularly with respect to the diminution of recurrences.

The majority of surgeons, however, treat pilonidal sinuses by excision with varying amounts of the surrounding tissue, and differ mainly in the method of closing the wound. Primary closure, open packing, and a number of modifications of these basic methods have been used but few are satisfied, either with the rate of recurrence or with the healing time. The principal drawbacks to primary closure are the constant presence of infection and the difficulty in obliterating the dead space. To overcome these disadvantages Ferguson and Mecray²⁹ defer operation until infection is controlled, and after the excision effect a careful closure which includes the use of retention sutures of alloy steel wire. The patient is then placed on his back on a litter or operating table for an hour to insure obliteration of any residual dead space. Gage³⁰ believes that operation should be deferred till six months after infection. He uses fine silk ligatures, does a primary closure, and applies a sea sponge under pressure to maintain the obliteration of the cavity. In his experience, silk ligatures have given better results

than catgut Dunphy,³¹ also, has advocated the use of silk and believes it reduces the number of recurrences Colp³² described a method of primary closure in which the flaps are mobilized, by undermining if necessary, and then sutured separately to the midline of the posterior sacrococcygeal ligament by interrupted mattress sutures of silk The skin edges are approximated with fine silk

Primarily concerned with obliteration of the dead space, Lahey,³³ in 1929, introduced an operation in which a flap with a single pedicle is raised from the adjacent skin and subcutaneous tissue and moved over into the

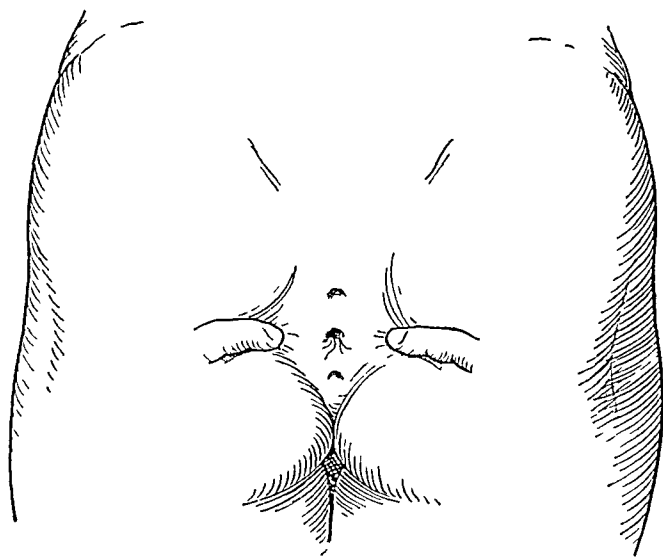


FIG 1—Typical appearance of pilonidal sinus, with hair projecting from middle sinus

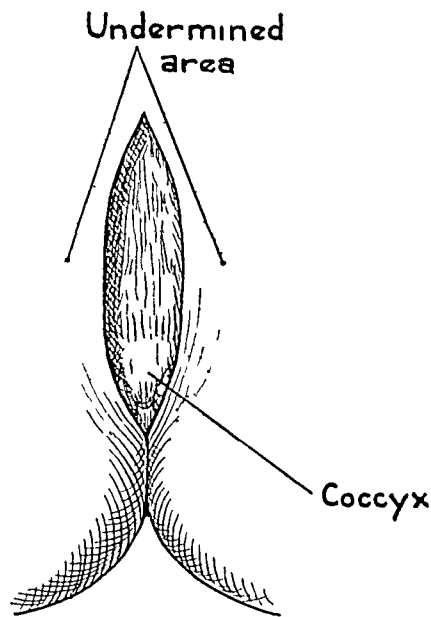


FIG 2—Sinus removed by block dissection, with undermining of skin and exposure of sacrococcygeal fascia

wound In 1932, Lahey³⁴ suggested that a flap be supported by two pedicles, one above and one below, instead of the original single pedicle above Swinton and Hodge³⁵ state that the modified operation is occasionally used at the Lahey Clinic, but limited block-excision with light packing is the common practice

The advantages of a successful primary closure are obvious—the healing time and the period of disability are greatly reduced A few surgeons have reported excellent results with primary closure but in most hands the method is disappointing The wound frequently fails to heal *per primam*, and often there is persistent drainage or recurrence

It is probable that the majority of surgeons in this country treat pilonidal sinuses on the principle of excision with open packing of the wound Believing that recurrences are fewer, they are willing to accept the prolonged healing time In a collected series, Kleckner³⁶ reported 4,699 cases, of which 4,231 had been operated upon by the open method

The results achieved with the standard methods of treatment show considerable divergence, as reported from various clinics and by individuals Gage,³⁰ for example, records 42 cases of excision, with primary closure,

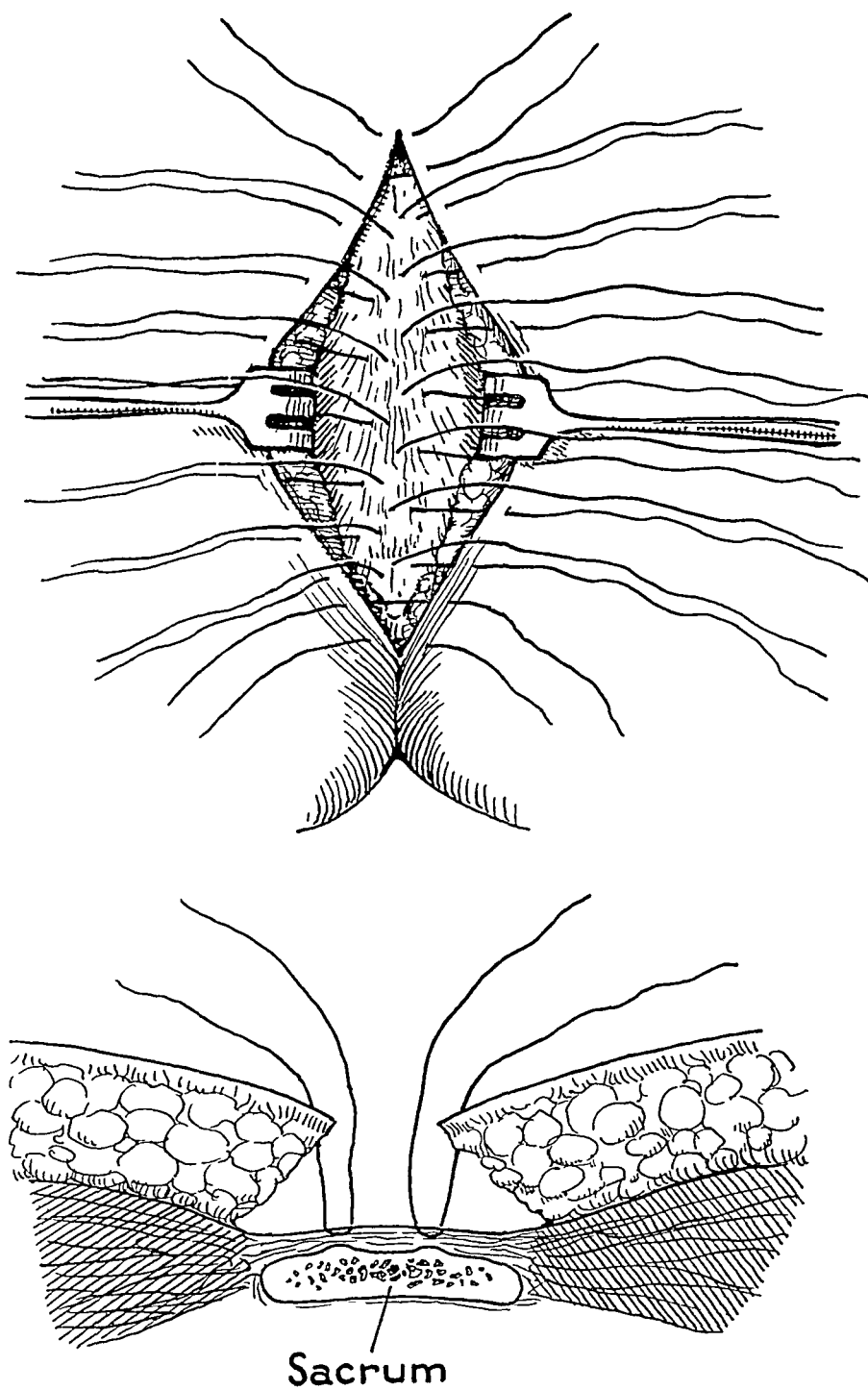


FIG 3—Sutures of black silk placed through skin edges and fascia ready for tying viewed from above and in cross section. In passing sutures through skin the subcutaneous fat is not included.

without a single recurrence, whereas in the cases reported by Rogers and Hall²⁷ the recurrence rate for primary closure was 36 per cent in the first series and 38 per cent in the second

In attempting to compare the results of primary closure with the open method the same difficulty is encountered In the large series collected by Kleckner³⁶ the incidence of recurrence was reported as 23.29 per

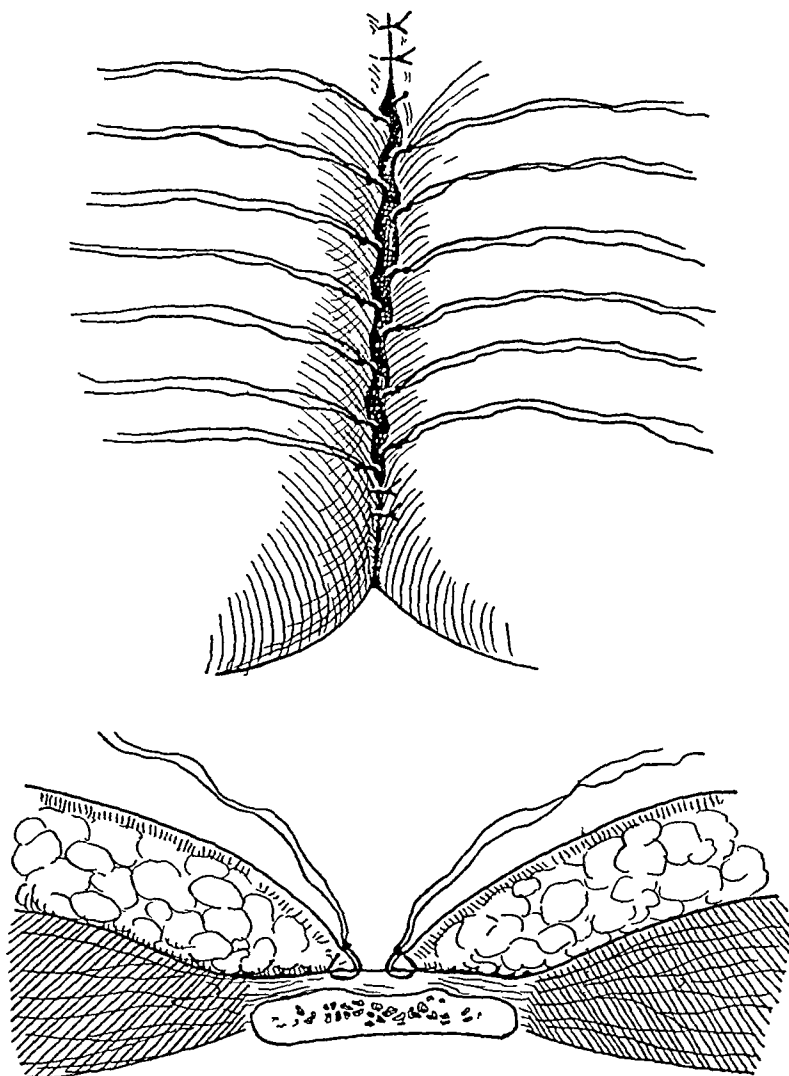


FIG. 4.—Sutures tied, bringing skin edges to fascia near mid line without tension

cent for primary suture and only 1.13 per cent for the open method Rogers and Hall²⁷ found recurrence rates of 18 and 25 per cent of the cases treated by open operation in their first and second series respectively In Kooistra's¹⁵ series the recurrence rates for primary closure and open packing were the same—21 per cent

The time required for healing of the operative wound is a matter concerning which complete data is not available The advocates of primary closure have emphasized the time factor when comparing this method with open packing, but usually do not take into account the cases that fail to heal by primary union Rogers and Hall²⁷ reported an average healing time of 2.7 months, approximately 82 days, following cautery excision In the series of 29 cases treated by excision and light packing, Swinton

and Hodge³⁵ found that 21 cases required 16 weeks, or 112 days to heal and the remainder up to one year. In Kooistra's cases, 24 treated by excision with packing required an average healing time of 90 days after leaving the hospital, in an equal number treated by primary closure the healing period was only 24 days. Two cases that were closed primarily but later opened and packed required 94 days to heal. Rogers²¹ has properly stressed the importance of the after-care of these cases, and believes it is important that the patient should remain under the treatment of the surgeon who has operated upon him.

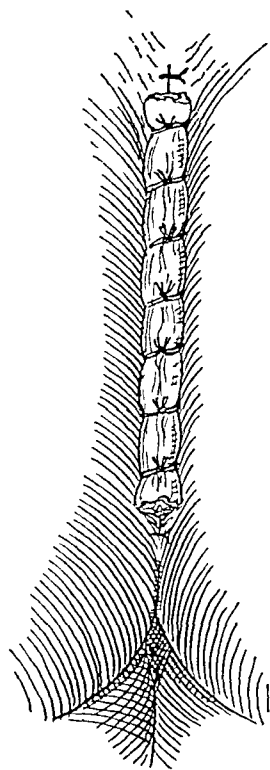


FIG 5—The ends of the sutures which have been left long are tied over a dressing roll of wet cotton or gauze as a convenient means of holding it in place. The wet dressing provides a capillary medium for the absorption of serious exudate.

The type of wound closure about to be described (Figs 1-5) has as its principal purpose the elimination of as much of the open wound as possible without the creation of a dead space. The tissue involved by the sinus is removed in the usual manner by block dissection, and partial wound closure is effected by suturing the skin edges to the sacrococcygeal fascia and underlying ligamentous structures. The skin edge on each side is brought as near the midline as possible without tension, and sutured with interrupted medium black silk, leaving a narrow uncovered area of fascia between. If this area is large enough to warrant it, a skin graft may be applied to further shorten the period of healing. A roll of gauze or cotton wet with normal saline solution is then applied to the wound, where it may be conveniently anchored by means of the suture ends which are left long to facilitate their subsequent identification and removal. If the wound can be kept clean it need not be disturbed for several days, but the dressing may be changed frequently if necessary. The sutures should not be removed until the skin has become firmly fixed to the fascia. This is usually a matter of 10 or 12 days.

Since January 1, 1936, 214 ward patients have been operated upon in New York Hospital for pilonidal sinus, with a total of 230 operations performed. The procedure described above was introduced at this hospital in 1936 and has since been carried out in 144 patients a total of 147 times, three of the patients having been operated upon twice. During the same period 36 operations with open packing, 34 with primary suture, and 12 incisions for the drainage of abscesses were performed. One other patient had a total of seven operations of various kinds and extent, and was not considered suitable for classification. With few exceptions the operations were performed by the resident staff. The treatment following discharge from the hospital was conducted in the Out-Patient Department with no particular group assigned to these cases.

The results of the various procedures are shown in Table I and are based upon operations performed rather than the number of patients operated upon. When a patient entered the hospital with a recurrence he was considered another case regardless of where the previous operation had been done. In reviewing the table, "cases" should be thought of as operations for pilonidal sinus rather than the number of patients involved. All cases including the simple incisions for drainage and the one not classified appear in the table.

The healing time is based upon the number of cases in which it could be definitely determined, and includes the days spent in the hospital after operation. Patients who had small granulating areas or slight discharge when last seen were not considered as healed. The numbers of cases upon which healing time is based are entered in parentheses.

TABLE I
THE RESULTS OF SURGICAL TREATMENT IN 230 CASES OF PILONIDAL SINUS

Type of Wound Closure	No of Cases	Average Postop Days in Hospital	Average Healing Time, in Days	Cured		Persistence or Recurrence		Result Unknown or Incomplete	
				No	Per Cent	No	Per Cent	No	Per Cent
Suture of skin edges to sacrococcygeal fascia	147	14	69, (89 cases)	97	66	19	12.9	31	21.1
Packing of open wound	36	25	118 (26 cases)	26	72.2	6	16.7	4	11.1
Primary suture	34	14	70 (23 cases)	22	64.7	11	32.3	1	2.9
Incision and drainage	12	7	153 (3 cases)	6	50	2	16.7	4	33.3
Unclassified	1					1			

The results with respect to cure and recurrence are based upon examinations in the Follow-Up Clinic. In a few instances information from sources considered reliable was accepted. No case was recorded as cured until followed for at least six months, the average time being 16 months. The term "cured" as applied to cases of incision and drainage should be interpreted as meaning free of symptoms for six months or more after operation. Patients who had a follow-up of less than six months were considered too recent for classification except in instances of recurrence. Percentages are based upon the total number of cases treated by each method as they appear in the first numerical column.

The average healing time following suture of skin edges to sacrococcygeal fascia was 69 days, for open packing it was 118 days, and for primary closure 70 days. Eighteen, or 53 per cent, of the 34 primary closures developed abscesses or other complications which greatly prolonged the healing time and raised the general average.

The patterns of wound healing in the cases with known healing time are shown in Charts 1, 2, and 3. The healing time is represented by the ordinates and the number of patients by the abscissas. In Chart 1 it will be observed that 47, approximately 52 per cent, of the 89 cases treated by suture of skin to fascia had healed within a period of 50 days, and 62, or 70 per cent, within 70 days. Chart 2, representing 26 cases treated by open packing of the wound, shows only 2 cases, approximately 8 per cent, healed within 50 days, and 9, approximately 35 per cent, healed within 70 days.

Chart 3, representing 23 cases treated by primary suture, shows that 14, approximately 61 per cent, had healed within 50 days, and 15, or 65 per cent, within 70 days. The numbers and percentages of cases requiring more than 150 days to heal were 6, or 6.7 per cent, for suture of skin to fascia, 6, or 23 per cent, for open packing, and 4, or 17 per cent, for primary closure. The figures dealt with are obviously too small to serve as a basis for conclusions but by providing an indication of healing tendencies in the three types of wound treatment they perhaps have a limited statistical value.

WOUND CLOSED BY SUTURE OF SKIN EDGES TO SACROCOCCYGEAL FASCIA—89 CASES

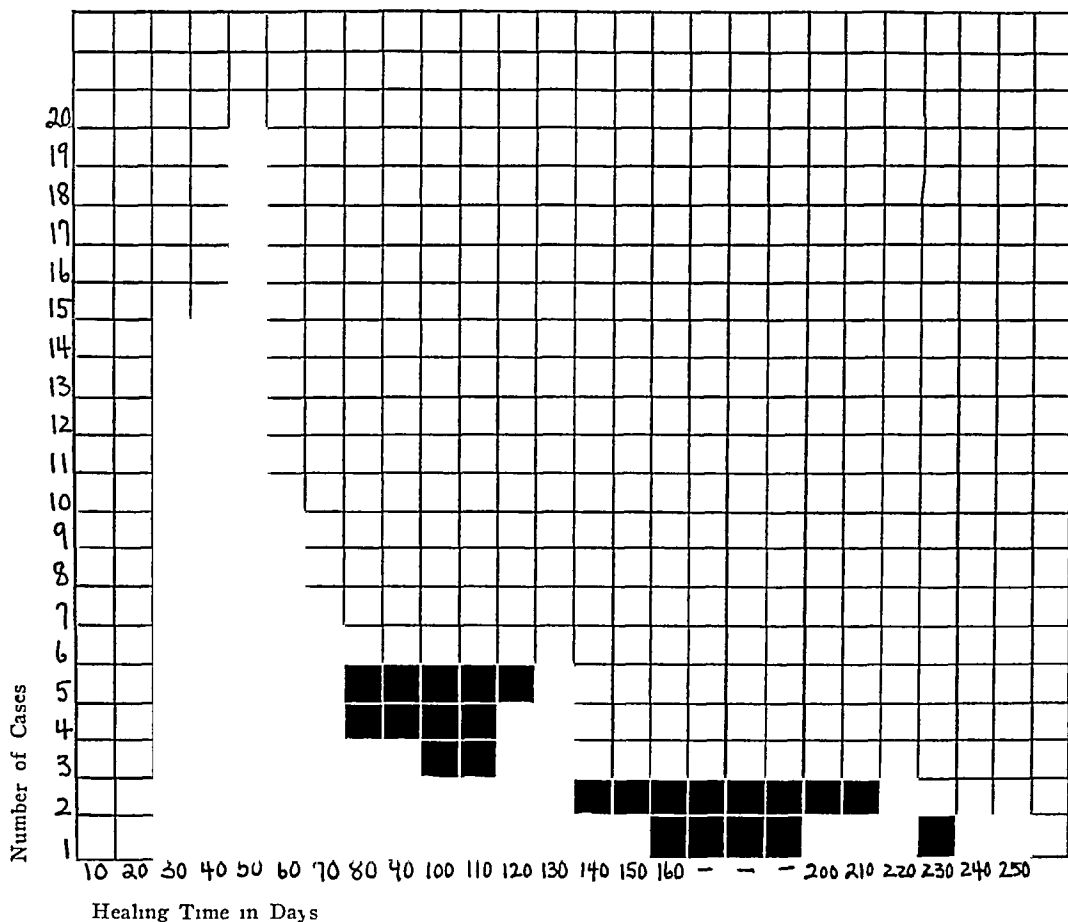


CHART 1—Healing pattern of wounds closed by suture of skin edges to sacroccocygeal fascia. The peak of healing was reached at 50 days, and the period in which the majority of cases healed was from 30 to 70 days.

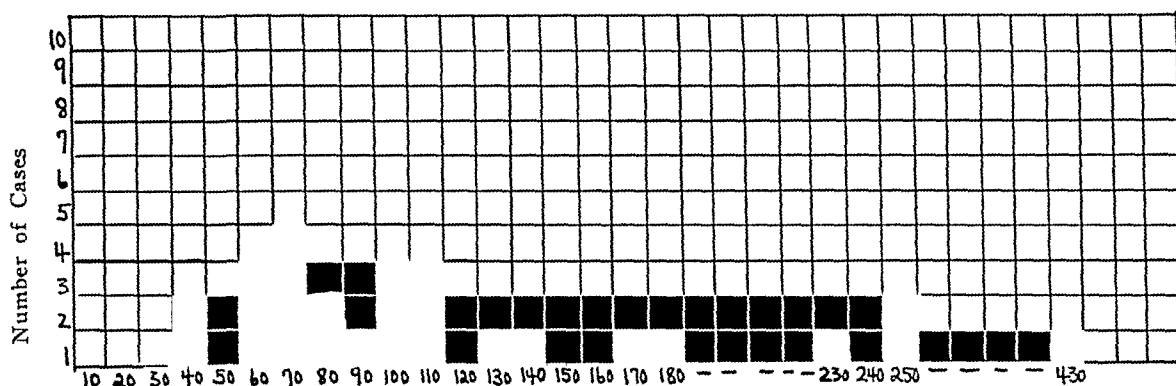
With respect to ultimate results, there were 19 known instances of recurrence or persistent drainage, 12.9 per cent, in the 147 cases of closure by suture of skin to fascia, 6, or 16.7 per cent, in 36 cases treated by open packing, and 11, or 32.3 per cent, in 34 cases closed by primary suture.

In this series the results of closure by suture of skin to fascia compare favorably in all respects with those of open packing and primary suture. The healing time following this operation is shorter than that generally recorded for the open operation. It is longer than the healing time for primary suture when primary suture is successful, but is shorter than that required

by the wound which has been closed by primary suture but subsequently opens and requires packing¹⁵

Recurrence or persistence of the disease following closure by suture of skin to fascia is less frequent than that reported by Dunphy,³¹ and Kooistia¹⁵

WOUND LEFT OPEN AND PACKED—26 CASES

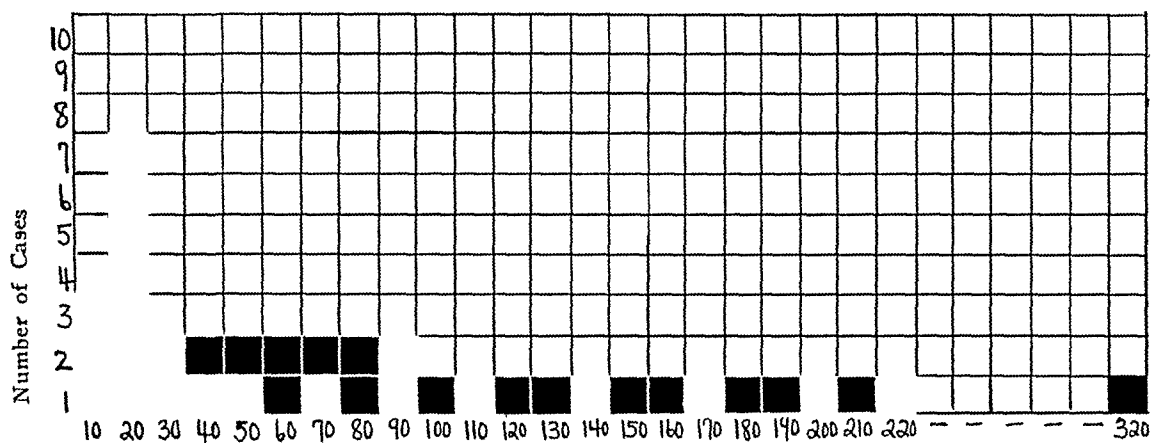


Healing Time in Days

CHART 2—The healing of wounds treated by open packing. The high point of healing was reached at 70 days. The period in which the majority of cases healed was from 60 to 110 days.

for primary closure and for open packing. It is much higher than Ferguson,²⁹ and Gage³⁰ report for primary closure, and higher than Rogers and Dwight²⁸ give for cautery excision with open packing. Rogers²¹ is convinced that many so-called recurrences are simply infected dead spaces due to faulty healing, and one must agree with him as to the importance of proper attention to the healing wound.

WOUND CLOSED BY PRIMARY SUTURE—23 CASES



Healing Time in Days

CHART 3—The healing of wounds closed by primary suture. The high point in healing was at 20 days, and slightly more than half the cases had healed within 30 days. The remainder failed to heal *per primam* and required varying lengths of time up to 320 days.

SUMMARY

- 1 The series consists of 214 patients upon whom 230 operations for pilonidal sinus were performed.
- 2 No two cases came from the same family.
- 3 There was no tendency toward association with other anomalies, but an incomplete spina bifida was present in one case.

4 The ratio of males to females was three to one

5 The series contains two Negroes, but no members of the yellow and brown races. Italians, Central Europeans, and Jews were the largest racial groups in a very mixed population

6 All cases presented evidence of infection, and half of them gave a history of one or more abscesses which had either been incised or had ruptured spontaneously

7 Thirty-two, or 15 per cent, had had one or more previous operations designed to bring about a cure

8 Only 13, or 6 per cent, of the 214 patients attributed the onset of symptoms to trauma

9 Five of the 57 female patients, 8.8 per cent, gave childbirth as the cause of onset, and two others stated that symptoms began during pregnancy

10 The youngest patient was 15 years of age and the oldest was 55. The average age of onset was 22.5 years, and the average age at the time of admission was 25 years. Four patients stated that the sinus had been observed at birth

11 A method of partial closure intended to reduce the healing time is presented and the results are compared with other methods of closure

12 The initial results are encouraging but the ultimate value of the method depends upon further experience with it

13 The postoperative care is important, both with respect to healing time and to the incidence of recurrence

REFERENCES

- ¹ Warren, J. M. Abscess Containing Hair on the Nates. *Am Jour Med Sc*, **28**, 113, 1854
- ² Warren, J. M. Surgical Observations with Cases. P 192, Ticknor and Fields, Boston, 1867
- ³ Anderson, A. W. Hair Extracted from an Ulcer. *Boston Med and Surg Jour*, **36**, 74, 1847
- ⁴ Keibel, F., and Mall, F. P. Human Embryology. Vol 2, pp 56-57, J. B. Lippincott & Co., Philadelphia, 1912
- ⁵ Kunitomo, K. The Development and Reduction of the Tail and Caudal End of the Spinal Cord. *Contributions to Embryology*, **8**, No 26, 161-198, 1918
- ⁶ Tourneau, F., and Herrmann, G. Sur la persistance de vestiges medullaires coccygiens pendant toute la periode foetale chez l'homme et sur le role de ces vestiges dans la production des tumeurs sacro-coccygiennes congenitales. *Jour de l'Anatomie et de la Physiologie*, **23**, 498-529, 1887
- ⁷ Mallory, G. B. Sarcrococcygeal Dimples, Sinuses, and Cysts. *Am Jour Med Sc*, **103**, 263-277, March, 1892
- ⁸ Gage, M. Pilonidal Sinus. An Explanation of its Embryologic Development. *Arch of Surg*, **31**, 175-189, August, 1935
- ⁹ Moise, T. S. Staphylococcus Meningitis Secondary to a Congenital Sacral Sinus. *Surg Gynec and Obstet*, **42**, 394-397, March, 1926
- ¹⁰ Ripley, W., and Thompson, D. C. Pilonidal Sinus as a Route of Infection in a Case of Staphylococcus Meningitis. *Am Jour Dis of Children*, **36**, 785-788, October, 1928

- ¹¹ Feré, C Cloisonnement de la cavité pelvienne, Uterus et vagin double, infundibulum cutane de la region sacro-coccygienne Bulletin de la Societe de l'Anatomie de Paris, 4th Serie, 3, 309-312, Mai, 1878
- ¹² Stone, H B Pilonidal Sinus ANNALS OF SURGERY, 79, 410-414, March, 1924
- ¹³ Stone, H B The Origin of Pilonidal Sinus ANNALS OF SURGERY, 94, 317-320, August, 1931
- ¹⁴ Fox, S L The Origin of Pilonidal Sinus Surg Gynec and Obstet, 60, 137-149, February, 1935
- ¹⁵ Kooistra, H P Pilonidal Sinuses Review of the Literature and Report of 350 Cases Am Jour Surg, 55, 3-17, January, 1942
- ¹⁶ Mechling, C C Congenital Proctologic Defects in Twins J A M A, 102, 367, February 3, 1934
- ¹⁷ Goldberg, S L, and Bloomenthal, E D Pilonidal Sinuses in Identical Twins J A M A, 113, 1401, October 7, 1939
- ¹⁸ Newell, R L Coccygeal Sinus Brit Jour Surg, 21, 219-228, October, 1933
- ¹⁹ Smith, M K Pilonidal Sinus and Cyst Christopher, F—Textbook of Surgery, pp 988-993, W B Saunders Co, Philadelphia, 1940
- ²⁰ Breidenbach, L, and Wilson, H L Pilonidal Cysts and Sinuses ANNALS OF SURGERY, 102, 455-463, September, 1935
- ²¹ Rogers, H The Treatment of Pilonidal Sinus in Hospital Practice New England Jour Med, 222, 79-82, January 18, 1940
- ²² David, V C Nelson New Loose-Leaf Surgery, Vol 5, Chapter 3, p 190, Thomas Nelson & Sons, New York, 1937
- ²³ Cutler, E C, and Zollinger, R The Use of Sclerosing Solutions in the Treatment of Cysts and Fistulae Am Jour Surg, 19, 411-418, March, 1933
- ²⁴ Block, L H, and Greene, B L Pilonidal Sinus Sclerosing Method of Treatment Arch Surg 37, 112-122, July, 1938
- ²⁵ Biegeleisen, H I Sclerotherapy for Pilonidal Cyst Am Jour Surg, 44, 622-625, June, 1939
- ²⁶ Rogers, H Pilonidal Sinus Surg Gynec and Obstet 57, 803-810, December, 1933
- ²⁷ Rogers, H, and Hall, M G Pilonidal Sinus Surgical Treatment and Pathologic Structure Arch Surg, 31, 742-766, November, 1935
- ²⁸ Rogers, H, and Dwight, R W Pilonidal Sinus Observations on 140 Cases Treated by Cautery Excision ANNALS OF SURGERY, 107, 400-418 March, 1938
- ²⁹ Ferguson, L K, and Mecray, P M Pilonidal Cysts Excision and Primary Suture in Ambulatory Patients Am Jour Surg, 36, 270-278, April, 1937
- ³⁰ Gage, M Pilonidal Sinus Transactions of the Southern Surgical Association, 1, 52-71, 1937, also ANNALS OF SURGERY, 109, 291-303, February, 1939
- ³¹ Dunphy, J E The Operative Treatment of Pilonidal Sinus With Special Reference to the Type of Suture Material as a Factor in Recurrence Surgery, 2, 581-584, October, 1937
- ³² Colp, R The Treatment of Pilonidal Cysts and Fistulae Surg Clin of North America, 9, 695-700, June, 1929
- ³³ Lahey, F H An Operation for Pilonidal Sinus Surg Gynec, and Obstet, 48, 101-111, January, 1929
- ³⁴ Lahey, F H A Further Suggestion for the Operative Treatment of Pilonidal Sinuses Surg, Gynec, and Obstet, 54, 521-523, March, 1932
- ³⁵ Swinton, N W, and Hodge, C C The Treatment of Pilonidal Sinus Surg Clin of North America, 19, 699-708, June, 1939
- ³⁶ Kleckner, M S Pilonidal Sinus Its Surgical Management Tr Am Proctological Soc, 37, 166-173, 1936

SUCCESSFUL CLOSURE OF AN ARTERIOVENOUS ANEURYSM INVOLVING THE LEFT INNOMINATE VEIN AND THE LEFT COMMON CAROTID ARTERY

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ARTERIOVENOUS ANEURYSMS are fairly common and rather easily recognized by the classic physical signs which are invariably present, with possible minor variations. We are presenting our experiences with an arteriovenous aneurysm which was unusual in its location. The difficulties encountered in the surgical correction of the condition were considerable. Our findings are analysed and a brief summary of the syndrome is presented.

Case Report—B J, Negro, male, age 31, was admitted to Grasslands Hospital, June 26, 1939. *Chief Complaint* Unilateral swelling and pain of left side of face of four months duration. *Past History* Essentially negative. Malaria as a child. History of luetic infection in 1934, with subsequent treatment. *Present Illness* Began January 17, 1939, when patient was stabbed in the chest. The White Plains Hospital reported a half-inch laceration of the skin, located about one-half inch below the sternal notch over the manubrium sterni, to the left of the midline, which was surrounded by a hematoma. The patient expectorated grayish blood-streaked sputum. The laceration was sutured and drained. The patient remained in the White Plains Hospital for four days, during which time roentgenograms of his chest were taken. He left the hospital against advice.

In February, 1939, about one month after the accident, the patient began to notice swelling of the left side of his face. Two weeks later he noted a buzzing in his left ear on turning his head to the left. He gradually developed shortness of breath which, on admission, had increased to the point where dyspnea was present on climbing two short flights of stairs. Shortness of breath was also initiated by lying on the left side. During the three months prior to admission, he had a cough productive of three to four ounces of thick sputum per day. The swelling of the left side of the face gradually became more marked and finally involved the left side of the neck. This swelling receded during the daytime, only to return during the night while the patient was lying down. During the weeks previous to his admission the buzzing in his left ear had become more annoying and was present most of the time. For three months previous to admission he had noted soreness under the upper sternum, aching pains down the left arm, and pain in the temporal region.

Physical Examination—**Positive Findings** On inspection, there was an obvious unilateral swelling of the left side of the face involving the left cheek, left lower eyelid, the temporal and parietal regions, and extended down over the mandibular region, and entire left side of the neck. The swelling was soft and did not pit. There was no exophthalmos, the pupils were equal and reacted normally, fundi were normal. On auscultation, a double bruit could be heard over the greater part of the swelling, but was loudest over the carotid region of the left side of the neck. The veins over the entire left side of the face, head and neck were swollen and distended. A palpable systolic thrill was present over both carotids, more marked on the left.

Examination of the chest showed an old, healed scar of the short, diagonal, three-quarter-inch stab wound over the manubrium sterni, slightly to the left of the midline, and about one inch below the sternal notch. The veins over the left side of the chest, left shoulder region, and entire left arm, as well as over the left upper portion of the abdomen were distended. A thrill, systolic in time, was felt over the entire cardiac area, but was most marked over the upper anterior chest. There was no pulsation in the sternal notch, no brassy cough, nor tracheal tug.

FIG 1



FIG 2

FIG 3

FIG 1—Six foot roentgenogram of the heart, September 24, 1936, two and one half years before the stabbing showing a normal heart and clear lung fields.

FIG 2—Roentgenogram of chest taken immediately following the accident, patient in prone position showing a marked widening of the mediastinum, especially superiorly.

FIG 3—Six foot roentgenogram taken in July, six months after the injury, showing a widening of the superior mediastinum and generalized cardiac enlargement.

The heart was enlarged in the transverse diameter. A loud, continuous murmur was heard over the entire precordium, which was loudest in the region of the scar. The quality and transmission of the diastolic murmur was very similar to that found in aortic insufficiency. The pulse was Corrigan in quality and there was a "pistol-shot" sound audible over the femoral vessels. Blood pressure 140/60, equal on both sides.

The left upper extremity, including forearm and hand was swollen, as compared to the right. The left arm measured $28\frac{1}{2}$ cm in circumference, 12 cm above the elbow, and $32\frac{1}{2}$ cm, 12 cm below the elbow. The right arm measured 28 cm in circumference, 12 cm above the elbow, and 32 cm, 12 cm below the elbow. Pulse

88-100, respirations 18-22, at rest The remainder of the physical examination was essentially negative

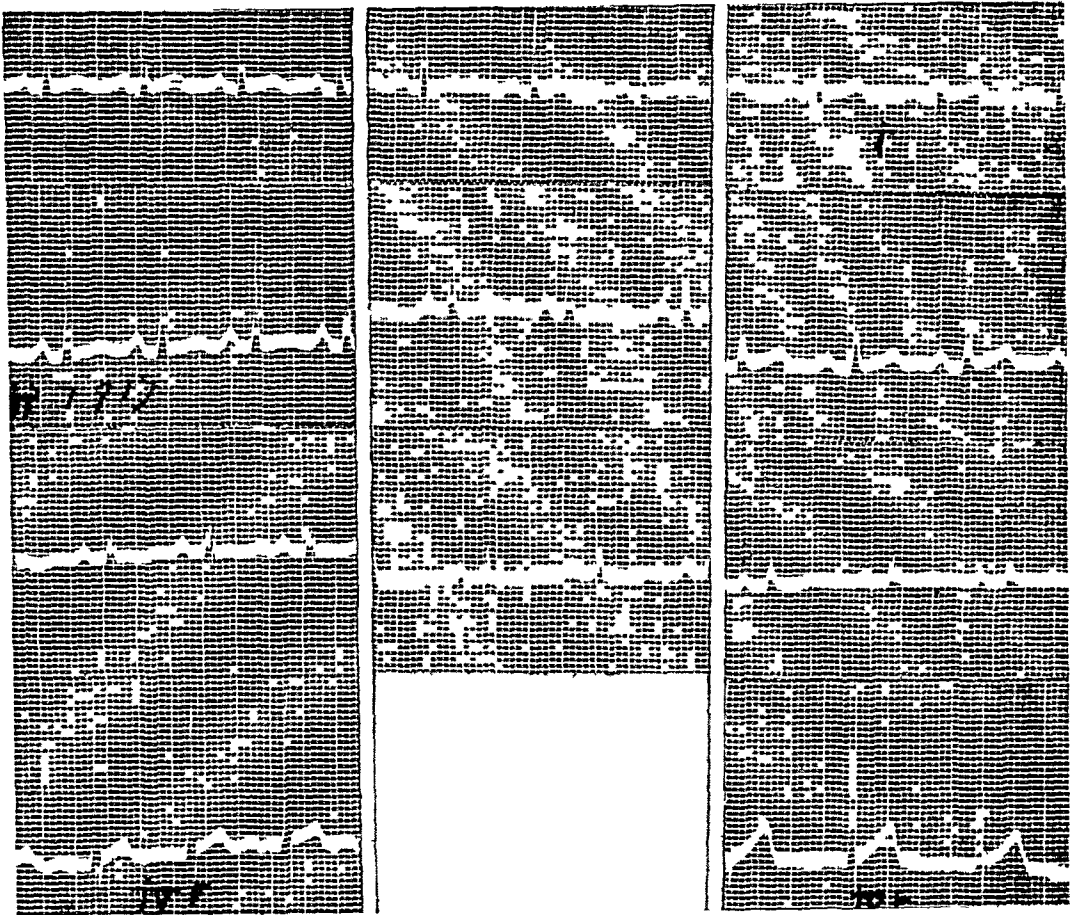
Laboratory Data—Venous pressure—left 35 cm (350 Mm) water, right 14 cm (140 Mm) water Circulation time (calcium gluconate)—left 19 seconds, right 16 seconds Wassermann and Kline tests negative Urine negative Hb 14.5 Gm RBC 4,550,000 WBC 4,700, differential count 52% neutrophils, 46% lymphocytes, 2% monocytes Blood sugar 80 mg NPN 25 mg CO₂ combining power—left arm 63, right arm 63

There had been occasion, in 1936, for a chest roentgenogram, which we were fortunate enough to obtain for comparison with the films made subsequent to the stabbing injury

7/5/39 A

7/29/39 B

9/22/39 C



GRAPH 1—Tracing A was taken two weeks preoperative. Tracings B and C were taken 11 days, and three months postoperative. The essential difference is in the height of the T waves. Those in tracing C are much higher than those of either A or B.

Roentgenologic Examinations—(1) The 1936 films showed the mediastinum of normal width, the heart was not enlarged, and there was no evidence of pleural fluid (Fig 1)

(2) The films taken January 17, 1939, directly after the accident showed marked widening of the mediastinal shadow, particularly in the upper portion (Fig 2)

(3) Films taken in July, six months after the injury, showed a widening of the superior mediastinum, and generalized enlargement of the heart (Fig 3)

An electrocardiogram, July 5, 1939, was within normal limits (Graph 1)

This case was investigated by the medical department and the diagnosis of arterio-venous aneurysm between the left innominate vein and the left common carotid artery

was arrived at. A surgical consultation was requested and the decision to operate was based on the following considerations:

First, for the relief of tinnitus, pain and swelling of the face and neck. Second, but most important, for the alleviation of the altered dynamics which had caused cardiac enlargement and disability that would undoubtedly have been progressive. It was felt that a sufficient length of time had elapsed to allow collateral circulation to be established, in case ligation was found to be necessary.

Operation—July 18, 1939. Under nitrous oxide, ether and oxygen anesthesia, with a closed system and endotracheal tube, a vertical midline incision was made from the midpoint (hyoid bone) on the neck, downward to the junction of the upper and middle thirds of the sternum. The sternum was divided in the midline from the sternal notch to the level of the third interspace. The sternal incision was carried to the left just below the third rib. The upper left sternal segment still attached to left clavicle, first, second, and third left ribs, was then elevated. The pleura was separated bluntly from the deep surface of the sternum and ribs. A mass completely filling the area, exposed by elevating that portion of the bony framework, obscured the structures beneath. Investigation of this mass, which was soft and pulsating, showed it to be made up of very friable tissue. It was ovoid in shape, and measured about seven centimeters in width and ten centimeters in length. By careful dissection below this mass the arch of the aorta was identified. The innominate vein, as such, could not be accurately demonstrated except at the distal end of the mass, where a structure resembling a dilated large vein coursed outwards beneath the clavicle. The internal jugular vein was identified in the lower neck close to the common carotid, and this vein was likewise dilated more than normal. It was concluded that this mass represented a pulsating aneurysm of an arteriovenous fistula between the left innominate vein and probably the left common carotid artery. In attempting to encircle the distal portion of the mass by blunt dissection for purposes of ligation, its wall was torn. Hemorrhage could not be controlled by suture-ligature because of the friable nature of the sac. A curved Kelly clamp, carefully applied over the rent, stopped the bleeding. A further attempt to separate the midportion of the sac from the aortic arch, in the hopes of applying a ligature in this location, resulted in a second tear which was controlled by a straight Kocher hemostat. At this point, digital pressure was applied in an attempt to find out if the communication between the artery and the sac could be obliterated. That portion of the sac overlying the proximal end of the carotid artery was squeezed between the fingers, and immediately the pulsation and thrill disappeared from the sac. The anesthetist observed that with the application of this pressure, the thrill in the upper neck abruptly ceased. It was then felt that if a ligature could be applied surrounding this portion of the sac, in all probability, the fistula would be obliterated. In spite of proceeding with extreme caution, to dissect a space to pass a ligature, a third opening was made into the sac, with rather brisk hemorrhage resulting. A straight Kocher clamp controlled this bleeding. It now became evident that it would be impossible to ligate, suture or transfix any portion of the mass. However, with the three clamps in place, hemorrhage was controlled and the fistula was apparently closed. Consequently, the clamps were left *in situ*, and iodoform gauze was packed around them. Dr Rudolph Matas¹ states that "The use of hemostatic clamps allowed to remain *in situ* have saved many lives, or at least bridged over many critical situations, when ligations were impracticable. I know this is true in my own experience." The elevated left upper chest wall was approximated to its other half, the clamps coming out through the opening in the sternum. The soft tissues were approximated, and the clamps bound securely together, and a suitable dressing applied.

Postoperatively, the patient had a fairly uneventful course. He developed a mild infection in the wound, probably because of the packing and clamps. On the twelfth day postoperative two of the clamps were carefully removed, without mishap. The third clamp was removed on the fourteenth postoperative day, with no untoward results.

The packing was removed bit-by-bit, and the infection treated

A roentgenogram, August 16, 1939, 30 days postoperative, showed a reduction in the size of the mediastinal shadow, as well as a reduction in the size of the heart to normal (Fig 4)

An electrocardiogram, July 29, 1939, 11 days postoperative, showed flattening of the T waves (Graph 1) By September 22, 1939 65 days postoperative, the T-waves had increased in amplitude to a point where they were higher than they were on July 5, 1939 (Graph 1)



FIG 4—Six foot roentgenogram, August 16, 1939, one month postoperatively showing narrowing of the superior mediastinum, and a reduction in the size of heart towards normal

FIG 5—Six foot roentgenogram, October 7, 1939, three months postoperative showing further narrowing of the superior mediastinum and a normal cardiac shadow

The patient continued to show improvement Some four weeks after operation a rather profuse, sudden hemorrhage occurred from the depths of the wound, but this was fairly easily controlled by packing Several minor episodes of bleeding occurred after this, and a low-grade infection persisted, but the wound slowly granulated A small abscess developed over the left upper chest, some seven centimeters from the main wound, which was incised and drained Cultures from this abscess showed *Staphylococcus albus*

On September 24, 1939, 67 days after operation the patient left the hospital against advice At this time the patient offered no subjective complaints He had no pain, or respiratory distress He felt no buzzing in his ear or head The swelling of the left face and head had completely disappeared There was no evident swelling of the left shoulder or left arm, though a slight fullness persisted in the left supraclavicular region The distended neck veins had receded to normal size The previously heard loud murmurs and cardiac thrill had disappeared A low systolic blowing murmur was heard at the apex, which was transmitted to the left axilla No bruit could be heard in the chest or in the neck The heart rate had slowed to 80, and less The blood pressure was approximately equal on both arms (left 98/70, right 100/74) Venous pressures—right 12.5 cm (125 Mm) water, and left, 30.5 cm (305 Mm) water

The patient was seen July 26, 1941, at which time he was working in a munitions factory lifting 75 to 100 lbs This caused him no discomfort Blood pressure 126/76 Pulse 78 No thrills or murmurs Fluoroscopy and electrocardiogram normal

DISCUSSION—Arteriovenous fistulae may be either acquired or congenital Both types produce local circulatory disturbances, and, if large enough,

profound systemic effects. The most common arteriovenous aneurysms are those involving the femoral, axillary, brachial, popliteal, carotid and subclavian vessels⁴. Our case is unusual, in that there is only one other recorded in which a fistula has connected the left internal carotid artery and the left innominate vein¹⁴. The other instance was overlooked during life, and was the ultimate cause of death.

The largest arteriovenous aneurysms are those connecting the aorta and the superior vena cava². They are practically always luetic in origin, and are invariably fatal within a short time. Recently, Burwell³ introduced the interesting conception of considering the placental circulation as an arteriovenous aneurysm. His points are well made and quite fascinating to contemplate. The most common congenital arteriovenous aneurysm is the patent ductus arteriosus.

The classic local signs of a continuous bruit and thrill, which are accentuated during systole and transmitted along the line of the vessels may be modified by the position of the arteriovenous aneurysm. In our case a diastolic thrill could not be felt, probably because of the chest thickness. The history of lues, the increased pulse pressure, Corrigan pulse, "pistol-shot" sound over the femoral arteries, and the character and transmission of the diastolic murmur made it necessary, for a while, to consider the possibility of a concomitant aortic valve lesion.

The local manifestations, in most instances, are of little consequence, a notable exception is the arteriovenous aneurysm involving the internal carotid artery and cavernous sinus, in which condition, the local changes greatly overshadow the systemic disturbances²¹. In the case herein presented, the patient sought relief for the local swelling, pain and bruit.

The systemic phenomena which may occur with an arteriovenous aneurysm are (1) An accelerated heart rate, (2) an elevation of the systolic arterial blood pressure and a lowering of the diastolic pressure, with a resultant increased pulse pressure, (3) an increased cardiac output, with a decreased stroke output, (4) engorgement of the pulmonary vessels, (5) an increased circulating blood volume, (6) cardiac enlargement, (7) electrocardiographic changes, and (8) increased venous pressure and circulation time, with the onset of cardiac decompensation^{3, 12, 17, 18, 19}. Where the fistula is accessible, compression will cause immediate slowing of the heart rate (Branham's sign), and a lowering of the systolic arterial blood pressure. These changes may be of assistance in evaluating the degree to which the arteriovenous aneurysm is influencing the general circulation. In some instances it has been possible to witness, under fluoroscopic examination, a clearing of the pulmonary fields upon digital obliteration of the shunt¹².

The position of the fistula in our case, precluded its compression before operation. Following surgical correction, however, the anticipated reversals were observed. The changes in heart size were the usual thing. The enlargement which occurs with arteriovenous fistulae is considered to be 75 to 90 per cent dilatation and 10 to 25 per cent hypertrophy⁷. The longer

the communication remains patent the more genuine hypertrophy develops and the less likely is complete reversibility possible¹⁷

The fullness of the left supraclavicular area, and the elevated venous blood pressure in the left upper extremity which have persisted after operation in our patient are, we feel, the result of a marked narrowing of the lumen of the left innominate vein. The cardiac rate has slowed from 88-100 to 78. The systolic blood pressure which was 140 before operation fell to 100 after operation, while the diastolic blood pressure rose from 60 to 70. While others have recorded improvement in the electrocardiographic picture following obliteration of the fistula, the changes in the T-waves noted here are perhaps more marked than usual¹⁹

The effects of an arteriovenous aneurysm are dependent upon the size of the fistula, the caliber of the vessels involved, the distance of the fistula from the heart, the volume and force of the arterial stream which is short-circuited, the age of the patient and his activity, and the presence or absence of coexistent cardiovascular disease^{9, 13, 15, 17}. Variations and combinations of the above factors explain the differences that one finds in the description of cases in the literature.

The time-honored surgical treatment for arteriovenous aneurysms has been a four-point ligation and removal of the fistula^{8, 9, 10}. The excellent results of Gross in the simple ligation of patent ductus arteriosus,¹¹ and our own end-result are evidence to the fact that radical procedures are not always necessary. Correction through transvenous arteriorrhaphy is frequently the method of choice¹⁶. In desperate situations, where cardiac decompensation is severe, one may have to resort to simple ligation of the proximal portion of the vein for temporary alleviation. The fact of the matter is that it is often impossible, and occasionally extremely dangerous, to perform a four-point ligation²⁰. Each instance of an arteriovenous aneurysm requires careful thought and precision in judgment as to the proper surgical procedure, the age of the patient, the duration of the aneurysm, the vessels involved, the type of fistula present, *etc*, will all influence the type of approach necessary, and very often the decision will have to be altered at the last moment to meet the findings disclosed at operation.

Unfavorable effects upon the general circulation are the usual indication for surgical intervention. Occasionally local changes alone may be troublesome or serious enough to require correction. In patent ductus arteriosus the question has arisen as to whether one is justified in ligating the fistula solely on the possibility that bacterial endocarditis may be obviated¹¹. The *Streptococcus viridans* has been known to lodge at the side of a traumatic arteriovenous aneurysm, causing all the signs and symptoms of a subacute bacterial endocarditis. Hamman and Rienhoff⁶ reported the surgical cure of such a case.

SUMMARY AND CONCLUSION

(1) A case of arteriovenous aneurysm involving the left innominate vein and the left common carotid artery is reported.

(2) The local and general manifestations of arteriovenous aneurysms are listed

(3) The method resorted to in the correction of the arteriovenous aneurysm reported in this paper, is described. This method is not advocated as an orthodox procedure but was dictated by the complications which arose

(4) The methods and indications for the correction of arteriovenous fistulae are mentioned

REFERENCES

- 1 Matas, Rudolph. Personal communication
- 2 Armstrong, E. L., Coggin, C. B., and Hendrickson, H. S. Spontaneous Arteriovenous Aneurysm of the Thorax. *Arch Int Med*, **63**, 298-217, February, 1939
- 3 Burwell, C. S., *et al*. Circulation During Pregnancy. *Arch Int Med*, **62**, 979-1003, December, 1938
- 4 Callander, E. L. Study of Arteriovenous Fistula. Analysis of 447 Cases. *ANNALS OF SURGERY*, **71**, 428, 1920
- 5 Gage, I. M., and Herrmann, G. R. Cardiac Hypertrophy in Arteriovenous Aneurysm. *Proc Soc Exper Biol and Med*, **25**, 765, 1928
- 6 Hamman, Louis, and Rienhoff, Wm. F., Jr. Subacute Streptococcus Viridans Septicemia—Cured by Excision of an Arteriovenous Aneurysm of the External Iliac Artery and Vein. *Bull Johns Hopkins Hosp*, **57**, 219, 1935
- 7 Herrmann, George, and Decherd, Geo. M., Jr. Some Studies in the Mechanism of Cardiac Hypertrophy. *Ann of Int Med*, **13**, No. 5, 794-807, 1939
- 8 Heirman, Louis G., and Reid, M. R. The Management of Arteriovenous Aneurysm in the Extremities. *Am J Surg*, **44**, 17-24, April, 1939
- 9 Holman, Emile. Arteriovenous Aneurysm. N. Y., Macmillan Co. 1937
- 10 Holman, Emile. Arteriovenous Aneurysm. *ANNALS OF SURGERY*, **80**, 801, 1924
- 11 Hubbard, J. P., Emerson, P. W., and Gross, H. Indications for Surgical Ligation of Patent Ductus Arteriosus. *New Eng Jour Med*, **221**, 481, September 28, 1939
- 12 LaPlace, L. B. Observations on the Effect of an Arteriovenous Fistula on the Human Circulation. *Am J Med Sc*, **189**, 497, 1935
- 13 Lewis, T., and Drury, A. N. Observations Relating to Arteriovenous Aneurysm Heart, **10**, 301, 1923
- 14 Mason, J. H. Traumatic Aneurysm of Great Vessels of Neck. *ANNALS OF SURGERY*, **109**, 735-748, May, 1939
- 15 Mason, J. M., Graham, G. S., and Bush, J. D. Early Cardiac Decompensation in Traumatic Aneurysm. *Am Surg*, **107**, 1029-1036, June, 1938
- 16 Matas, Rudolph. Some Experiences and Observations in the Treatment of Arteriovenous Aneurysms by the Intravascular Method of Suture (Endo-aneurysmorrhaphy) With Special Reference to the Transvenous Route. *ANNALS OF SURGERY*, **71**, 403, 1920
- 17 Porter, W. B., and Baker, J. B. The Significance of Cardiac Enlargement Caused by Arteriovenous Fistula. *Ann Int Med*, **11**, 370, 1937
- 18 Price, G. B. Cardiovascular Changes Following Aneurysm. *Lancet*, **1**, 206-207, January 23, 1937
- 19 Quattlebaum, J. T. Case with Pronounced Electrocardiographic Changes. *Am Heart J*, **13**, 95-103, January, 1937
- 20 Reid, M. R., and McGuire, J. Arteriovenous Aneurysms. *ANNALS OF SURGERY*, **108**, 643-693, October, 1938
- 21 Singleton, Albert O. Intracranial Arteriovenous Aneurysms. *ANNALS OF SURGERY*, **110**, 525-543, October, 1939

A COMPLICATED CASE OF ANEURYSM INVOLVING THE ILIAC AND FEMORAL ARTERIES

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THE FOLLOWING CASE of iliofemoral aneurysm is reported because of several unusual features which complicated its management

Case Report—C C H No 145047 The patient, F F, came under observation May 26, 1941 He gave the history that 38 years ago he had been shot through the inner aspect of his left thigh An "aneurysm," probably an arteriovenous fistula, developed at the site of the wound and was excised Three years later a pulsating mass in the left groin spontaneously appeared During the past 35 years this mass had slowly increased in size and was becoming painful In addition, he was suffering from chronic ulceration of the leg, intermittent claudication, and extreme coldness, numbness, and cyanosis of the foot

Physical Examination—White male, age 60 The left foot was extremely cyanotic, cold to the touch and moist On elevating the limb the sole of the foot became pale Atrophy and ulceration of the skin of the lower two thirds of the leg were present Pulsation was barely palpable in the dorsalis pedis and posterior tibial arteries, and oscillometric examination revealed only a trace of pulsation in the region of the lower leg There was a depressed linear scar six inches in length overlying the course of the subsartorial canal in the thigh, and no arterial pulsation was palpable in this region

The common femoral and external iliac arteries had been converted into a large, painful, vigorously pulsating, fusiform aneurysmal mass The aneurysm was constricted by the overlying ilio-inguinal ligament giving it a dumb-bell shape The femoral component of the aneurysm measured four inches in its external diameter Serologic tests for syphilis were negative

To evaluate what role vasospasm played in the evident ischemia of the foot and leg, skin temperature readings were taken before and after a procaine block of the posterior tibial nerve At a room temperature of 26° C, the nerve block was followed by a rapid rise in the surface temperature of the fifth toe and adjacent sole, from a stabilized level of 25° C to a vasodilation level of 32° C, and the cyanosis of the toes was replaced by a healthy pink color (Chart 1)

Because of this obvious vasospasm, it was deemed advisable to precede excision of the aneurysm by a lumbar sympathectomy It was felt that permanent relaxation of these spastic vessels would expedite the growth of a distal collateral circulation and constitute a protection against gangrene of the ischemic foot which, in the absence of a superficial femoral artery, might otherwise follow excision of the external iliac and common femoral arteries Accordingly, on June 11, 1941, through a muscle-splitting extraperitoneal approach, the left lumbar sympathetic trunk was divided at the upper margin of the third lumbar vertebra, stripped for a length of four inches, and buried in the adjacent psoas muscle^{1,2} The following day, the foot and leg were hot, red, and dry Figure 1 shows the external appearance of the femoral portion of the aneurysm several weeks following sympathectomy

At the time of his second admission to the hospital, four months following the sympathectomy, it was noted that the foot and leg were now pink and warm and that the ulceration had healed Oscillometric readings taken at the level of the lower leg had increased from a preoperative value of one-half to one and one-half The aneurysm had reached alarming size

On October 13, 1941, the femoral portion of the aneurysm was exposed through a vertical incision. Distally, the aneurysmal sac terminated in a fibrosed, cord-like structure which, on further dissection, proved to be the proximal remains of the previously resected superficial femoral artery. The deep femoral artery, which exhibited strong pulsation, emerged from the posterior aspect of the lower portion of the sac. On mobilizing the lateral margin of the sac, the femoral nerve was observed to be imbedded in the wall of the aneurysm. Resection of the sac could not have been accomplished without injury to the femoral nerve. A length of umbilical tape was passed around the sac just above the orifice of the deep femoral artery and tied

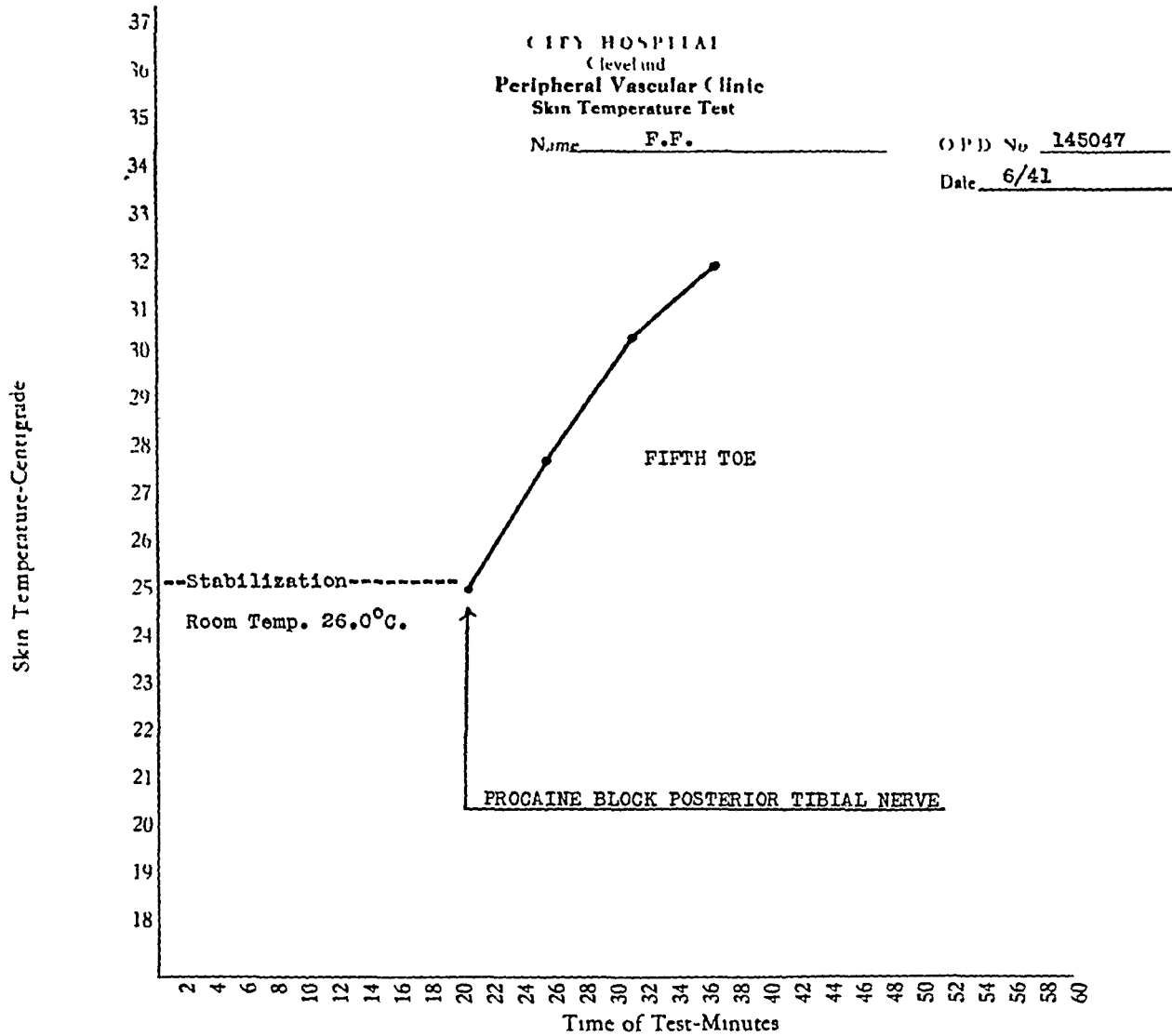


CHART 1—Depicting the rapid rise in the skin temperature following temporary interruption of the flow of sympathetic nervous impulses to the vasospastic foot

Pulsation in the deep femoral artery promptly disappeared, and there was a distinct diminution in the vigor of pulsation within the aneurysm itself. Nutrition of the foot was maintained.

On October 27, 1941, the iliac portion of the aneurysm was exposed through a supra-inguinal extraperitoneal approach, similar to that conventionally employed to expose the lower end of the ureter. The aneurysm extended up to the origin of the internal iliac artery. A ligature of umbilical tape was placed just distal to the origin of this artery, and the entire aneurysmal portion of the external iliac together with the accom-

panying vein were excised down to their disappearance into the thigh (Figure 2 is a diagrammatic representation of the operative findings and procedure) Microscopic examination of the resected portion of the aneurysm revealed arteriosclerosis to be the basic pathology Pulsation within the residual femoral portion of the aneurysm sac promptly disappeared By the time of his discharge, the sac had completely thrombosed The foot remained pink and warm

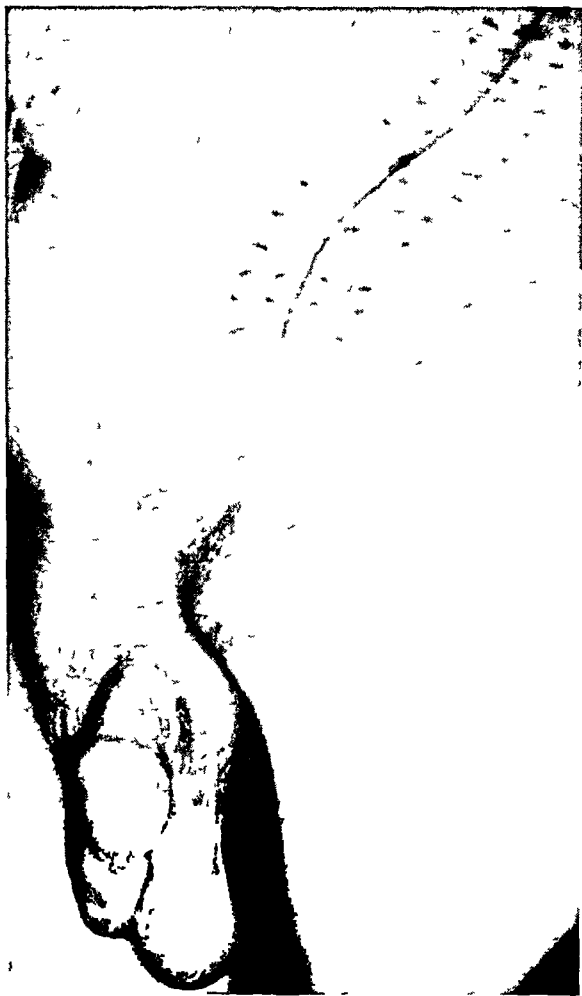


FIG 1—Showing the external aspect of the femoral portion of the aneurysm Note the recently healed Pearl type of incision employed to expose the lumbar sympathetic trunk There is an associated right inguinal hernia

Six months later the foot was pink and warm, and in an excellent state of nutrition The leg ulcers had remained healed There were no symptoms of ischemia other than a mild degree of intermittent claudication The residual portion of the aneurysm had been converted into a fibrosing, nonpulsatile mass which had already shrunk to about one-quarter of its original size

COMMENT—It is the opinion of Sir Thomas Lewis,^{3, 4} based on the work of Thoma,⁵ and Nothnagel,⁶ that the development of a collateral circulation is a true hyperthrophic response to an increase in the volume rate of blood flow through the auxiliary channels This increase in blood flow is, in turn, a physiologic response to a diminution in the peripheral resistance to blood flow resulting from a relaxation of the arteriolar-capillary bed within the ischemic part

Leriche,⁷ and his coworkers, were able to experimentally demonstrate in dogs how sympathetic vasoconstrictor impulses inhibit the spontaneous development of a collateral circulation following resection of the bifurcation of the

abdominal aorta

Working with selected cases of arteriosclerotic disease of the lower extremities, I⁸ have been able to demonstrate that there is a slowly progressive increase in the magnitude of measurable arterial pulsation in the region of the lower leg over a period of 6–12 months following lumbar sympathectomy For reasons stated in the original communication, these observations can be explained only on the basis of a development of a collateral circulation in response to the surgically induced relaxation of the peripheral small vessel bed

The reported case supports this conception that increased sympathetic vasoconstrictor tone may play an important rôle in the failure of a collateral circulation to spontaneously develop following a major arterial block. For 35 years this patient had suffered from severe ischemia of a foot and leg incident to excision of his superficial femoral artery. Ordinarily, in the

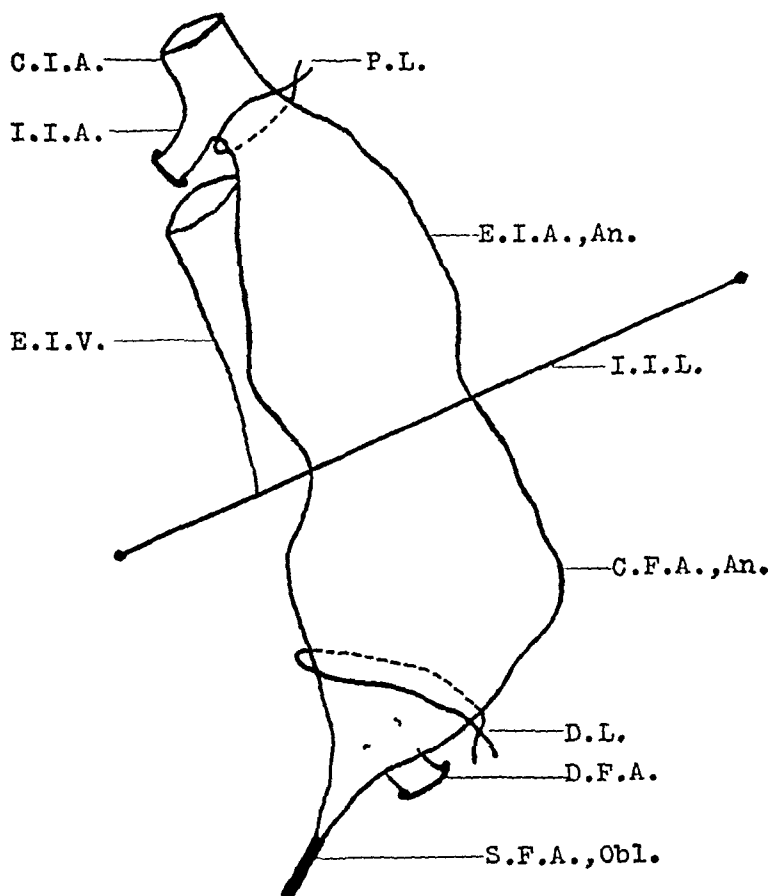


FIG 2—Diagrammatic sketch of operative findings and procedure

C I A	Common iliac artery
I I A	Internal iliac artery
P L	Proximal ligature
E I V	External iliac vein, excised along with
E I A	Aneurysmal external iliac artery
I I L	Ilio inguinal ligament
C F A	Aneurysmal common femoral artery
D L	Distal ligature
D F A	Deep femoral artery
S F A	Obliterated remnant of superficial femoral artery

absence of other peripheral arterial disease, excision of this artery does not produce such prolonged disability. The inadequacy of the collateral circulation in this instance can be best explained on the inhibiting influence of the associated vasospasm. To have thrown an added burden on this meager collateral circulation by primarily excising and thrombosing the aneurysmal iliofemoral artery would surely have resulted in gangrene of the foot and leg. For that reason it is believed that the lumbar sympathectomy was a crucial maneuver in the maintenance of an adequate blood supply to the foot and leg.

It is interesting to speculate on the anatomy of the ultimate collateral circulation present in this case. The net-result of the arterial surgery performed on this patient was equivalent to a total ablation of the main arterial

supply of a lower extremity Beginning at the origin of the external iliac artery, it included the total lengths and all the orifices of their branches of the external iliac, the common femoral, and the superficial femoral arteries The collateral circulation to the foot and leg must have its origin then in the buttock and posterior aspect of the thigh through anastomoses between the gluteal branches of the internal iliac artery and the perforating branches of the deep femoral artery, and, finally, through communications between the latter and the geniculate branches of the popliteal artery

REFERENCES

- ¹ Atlas, L N A Modified Form of Lumbar Sympathectomy for Denervating the Blood Vessels of the Leg and Foot ANNALS OF SURGERY, **111**, 117, 1940
- ² Atlas, L N Sympathetic Denervation Limited to Blood Vessels of Leg and Foot, II ANNALS OF SURGERY, **116**, 476, September, 1942
- ³ Lewis, Sir T Adjustment of Blood Flow in Arteriovenous Fistula Clin Sci, **4**, 277, 1940
- ⁴ Lewis Vascular Diseases of the Extremities Macmillan Co, New York 1936
- ⁵ Thoma Virchow's Arch, **95**, 294, 1884
- ⁶ Nothnagel Collateral Circulation Formation Ztschr f klin Med, **15**, 42, 1889
- ⁷ Leriche, R Surgery of Pain Williams and Wilkins, Baltimore 1939
- ⁸ Atlas, L N Lumbar Sympathectomy in the Treatment of Selected Cases of Peripheral Arteriosclerotic Disease Am Heart Jour, **22**, 75, 1941

A COMPARISON OF THE RESULTS OF ROENTGEN RAYS, SULFANILAMIDE AND SERUM THERAPY IN EXPERI- MENTAL GAS GANGRENE IN THE PIGEON

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THE PROBLEM of the management of wounds contaminated with the *Clostridium welchii*, and associated organisms, is not as yet settled. Numerous communications by Kelly^{1, 2, 3, 4, 5, 6, 7} would lead one to believe that roentgenotherapy affords a specific with which to treat such lesions. In a review⁸ of 222 cases of gas gangrene following trauma collected from the literature between 1930 and 1936, 41 cases were treated with roentgen rays and serum, with a mortality of 19 per cent, 124 were treated with serum alone, with a mortality of 17 per cent, and 57 received neither roentgen rays or serum, and had a mortality of 31 per cent. These data led us seriously to question the value of roentgenotherapy. The following experiments on pigeons were undertaken several years ago to determine whether roentgen rays would prove beneficial in experimental *Cl. welchii* infection. At the same time, the opportunity presented itself to determine the effect of sulfanilamide on similarly inoculated pigeons.

The strain of *Clostridium welchii* used in these experiments was isolated from a patient admitted to the Philadelphia General Hospital, November 2, 1937, 30 hours after a gunshot injury of the left forearm, which was self-inflicted. On admission, the clinical diagnosis of gas gangrene was made and later confirmed by bacteriologic study. The use of this strain minimized the possibility of strain specificity to which one might attribute the results obtained from use of serum if a laboratory strain had been used. The patient recovered following the use of serum and roentgenotherapy, and delayed amputation. The conscientious surgeon naturally hesitates to withhold any agent which may be of benefit to the patient. The multiplicity of therapeutic methods which are frequently employed on patients with gas gangrene makes it difficult to obtain satisfactory data as to the specificity of any one agent.

Technic—A chopped meat proteose-peptone broth, with 5 per cent dextrose, was inoculated from the stock culture and incubated under anaerobic conditions for 16 hours. A subculture from this was made and incubated for five hours. Five cubic centimeters of the culture were then taken and centrifuged for 20 minutes. The supernatant fluid, containing most of the toxin, was removed. The bacteria were resuspended in 15 cc of normal saline and again centrifuged. This was repeated once. Finally, the bacteria were again resuspended in 15 cc of saline, thus having a washed 1:3 dilution of a five-hour culture. In this way virulent organisms were obtained.

with a minimum amount of toxin present. The breast of each pigeon used in these experiments was injected with 0.5 cc. of this bacterial suspension.

Bull and Pritchett⁹ had recommended the use of the pigeon, and we found it to be an excellent laboratory animal. All experiments were carried out in groups of 25 pigeons. These were subdivided into groups of five, so that in each experiment five groups, treated by different methods and inoculated from the same subculture were compared. In all experiments one group was used as a control. The pigeons varied in weight from 7 to 16 ounces. There seemed to be no relation between weight of pigeon and chance of recovery. The average weight of the ones that died was 11.1 ounces, while in those that lived it was 10.7 ounces. The smallest pigeon, weighing seven ounces, recovered following the use of serum.

RESULTS

Table I gives the results obtained in each experiment. They are consistent throughout and show only slight variations between groups. Table II is simply a summary of Table I.

Control—In the control group of 30 pigeons, 63 per cent were dead within 10 to 12 hours. Only two birds survived one week, at which time the experiment was terminated. It was noted in this group, as in all others, that the birds tended to die within 24 hours and if they survived 24 hours, permanent survival was a likely possibility.

Serum-Treated Group—The serum used in these experiments was unconcentrated horse serum and contained 300 units to one cubic centimeter. In each instance 0.5 cubic centimeter was injected into the left breast of the pigeon. This dosage of 150 units would compare roughly by weight to 40,000 units in a 150-pound man. The time of injection of the serum varied from 35 to 142 minutes after inoculating the pigeon with organisms. The average time was 83 minutes.

There was some variation in average time elapsing between inoculation and injection of the serum in the six experiments. In Experiment 1, the average time was 75 minutes, Experiment 2, 72 minutes, Experiment 3, 38 minutes, Experiment 4, 137 minutes, Experiment 5, 110 minutes, and Experiment 6, 66 minutes. Mortality was not increased by delaying the injection of serum within these time limits.

In the pigeon, serum was by far the best therapeutic agent. Only one of the 30 pigeons died within 10 to 12 hours, while 19 of 30 in the control group died in this time. Nineteen pigeons, or 64 per cent of the serum-treated pigeons, survived. It is possible that a still higher percentage of survivals could have been obtained had the injection of serum been repeated in 24 hours. That this is a specific effect, and not due to a non-specific serum reaction, is shown by experiments with normal horse serum and bovine pneumococcic serum. With the bovine serum the final mortality was 100 per cent. In Experiment 5, normal horse serum appeared to give some protection.

THERAPY OF GAS GANGRENE

Sulfanilamide-Treated Group—Fifteen pigeons received sulfanilamide by mouth following inoculation. The sulfanilamide was mixed with 5 per cent gum acacia, so that each cubic centimeter of mixture contained 100 milligrams of sulfanilamide. Each pigeon in the group received 100 mg immediately after injection, while in Experiments 2 and 3 another 100 mg

TABLE I

Treatment and Experiment No	10-12 Hours			24 Hours			48 Hours			1 Week		
	Alive	Dead	Mor- tality %	Alive	Dead	Mor- tality %	Alive	Dead	Mor- tality %	Alive	Dead	Mor- tality %
Control												
1	2	3	60	0	5	100	0	5	100	0	5	100
2	2	3	60	1	5	80	1	4	80	1	4	80
3	3	2	40	1	4	80	0	5	100	0	5	100
4	1	4	80	0	5	100	0	5	100	0	5	100
5	1	4	80	1	4	80	1	4	80	0	5	100
6	2	3	60	1	4	80	1	4	80	1	4	80
	—	—	—	—	—	—	—	—	—	—	—	—
	11	19	63	4	26	86	3	27	90	2	28	93
Serum												
1	5	0	0	3	2	40	2	3	60	2	3	60
2	5	0	0	4	1	20	3	2	40	2	3	60
3	5	0	0	5	0	0	4	1	20	4	1	20
4	5	0	0	5	0	0	5	0	0	5	0	0
5	5	0	0	5	0	0	4	1	20	4	1	20
6	4	1	20	4	1	20	2	3	60	2	3	60
	—	—	—	—	—	—	—	—	—	—	—	—
	29	1	3	26	4	13	20	10	33	19	11	36
Sulfanilamide												
1	2	3	60	2	3	60	1	4	80	0	5	100
2	4	1	20	2	3	60	1	4	80	0	5	100
3	1	4	80	0	5	100	0	5	100	0	5	100
	—	—	—	—	—	—	—	—	—	—	—	—
	7	8	53	4	11	74	2	13	86	0	15	100
X ray prophylactic												
1	5	0	0	1	4	80	0	5	100	0	5	100
2	1	4	80	0	5	100	0	5	100	0	5	100
3	3	2	40	2	3	60	1	4	80	1	4	80
4	0	5	100	0	5	100	0	5	100	0	5	100
	—	—	—	—	—	—	—	—	—	—	—	—
	9	11	55	3	17	85	1	19	95	1	19	95
X-ray therapy												
1	3	2	40	0	5	100	0	5	100	0	5	100
2	3	2	40	2	3	60	2	3	60	1	4	80
3	2	3	60	0	5	100	0	5	100	0	5	100
4	1	4	80	1	4	80	1	4	80	1	4	80
	—	—	—	—	—	—	—	—	—	—	—	—
	9	11	55	3	17	85	3	17	85	2	18	90
X-ray and serum												
4	3	2	40	3	2	40	3	2	40	3	2	40
5	5	0	0	5	0	0	4	1	20	3	2	40
6	4	1	20	3	2	40	1	4	80	1	4	80
	—	—	—	—	—	—	—	—	—	—	—	—
	12	3	20	11	4	26	8	7	46	7	8	53
Normal horse serum												
5	3	2	40	3	2	40	3	2	40	3	2	40
6	0	5	100	0	5	100	0	5	100	0	5	100
	—	—	—	—	—	—	—	—	—	—	—	—
	3	7	70	3	7	70	3	7	70	3	7	70
Pneumococcic serum												
5	1	4	80	0	5	100	0	5	100	0	5	100
6	1	4	80	0	5	100	0	5	100	0	5	100
	—	—	—	—	—	—	—	—	—	—	—	—
	2	8	80	0	10	100	0	10	100	0	10	100

were given five hours later Pigeons that survived until the following morning received 100 mg of sulfanilamide twice daily until death No beneficial effect was noted from sulfanilamide given in this manner There were no permanent survivals There is one definite criticism of this method, namely, we have no evidence to offer that the sulfanilamide given these birds was absorbed A recent publication by Bieter, Baker, Beaton, Shafter, Seery and Orr¹⁰ indicates that sulfanilamide administered to chickens in doses similar to those employed by us will afford blood concentrations well above 10 mg per cent

 TABLE II
 SUMMARY

Treatment	Total Number of Animals	10-12 Hours Mortality		24 Hours Mortality		48 Hours Mortality		1 Week Mortality	
		No	%	No	%	No	%	No	%
Control	30	19	63	26	86	27	90	28	93
Serum	30	1	3	4	13	10	33	11	36
Sulfanilamide	15	8	53	11	74	13	86	15	100
X-ray prophylactic	20	11	55	17	85	19	95	19	95
X-ray therapy	20	11	55	17	85	17	85	18	90
X-ray and serum	15	3	20	4	26	7	46	8	53
Normal horse serum	10	7	70	7	70	7	70	7	70
Pneumococcic serum	10	8	80	10	100	10	100	10	100

Prophylactic Roentgenotherapy—Irradiation was given five to six hours before the injection of organisms In Experiments 1 and 2, 75 r were given with a one millimeter aluminum filter at 30 cm distance The rays were generated at 130 Kv 8 ma The portal was large enough to cover the entire pigeon Treatment lasted 15 minutes In Experiment 3, 160 r were given and in Experiment 4, 200 r were given No difference could be noted between the reactions of this group and the control group to inoculation by the *Clostridium welchii* In the 20 pigeons thus treated there was only one survival at the end of the week, or a mortality of 95 per cent, in comparison to 93 per cent in the control group

Therapeutic Roentgenotherapy—The filter and the distance were the same as in the prophylactic roentgenotherapy group In Experiment 1, 75 r were given 50 minutes after inoculation, in Experiment 2, 100 r were given 40 minutes after inoculation, and in Experiments 3 and 4, 160 r were given 20 minutes and five hours, respectively, after inoculation The eventual mortality in this group was 90 per cent, and no difference could be noted between the reactions of this group and the control group to inoculation by the *Clostridium welchii* In the 20 pigeons thus treated there was only one survival at the end of the week, or a mortality of 95 per cent, in comparison to 93 per cent in the control group

Roentgenotherapy and Serum—Although roentgen ray alone had no effect on the infection in pigeons, it seemed possible that a higher percentage of survivals might be obtained by employing roentgenotherapy in conjunction with serum Using the amount of serum previously described, plus irradiation, a consistently higher mortality occurred than when serum

alone was administered. In Experiment 4, 200 r were given 29 hours before inoculation and serum was administered two hours after inoculation. In Experiment 5, 200 r were given one hour after inoculation and the serum three hours after inoculation. In Experiment 6, 200 r were given 45 minutes after inoculation and the serum one hour after inoculation. The mortality at the end of one week in this group was 53 per cent, while when serum alone was used the mortality was but 36 per cent.

DISCUSSION—Experimental and clinical evidence is somewhat contradictory on the value of the various therapeutic agents in gas gangrene. Caldwell¹¹ concluded that roentgenotherapy has no effect upon the progress of a fulminating type of gas gangrene, but does bring about some localization of the process when given one to two hours after inoculation, and when the animals (guinea-pigs) survive 48 hours or longer. He obtained three survivals in a group of 10 animals, while the four controls all died. In a later article, Caldwell and Cox¹² concluded, from an experimental study on some 400 guinea-pigs, that roentgenotherapy is only of slight value. However, Williams and Hartzell,¹³ in two comparative clinical series of 12 cases each, had only one fatality in those patients treated with roentgenotherapy, and seven fatalities in those which failed to receive roentgenotherapy. One must remember that clinical cases of gas gangrene usually have a mixed infection, and it is possible that the beneficial effects of irradiation were due to the effect of the roentgen rays on organisms other than the *Clostridium welchii*. Against this theory are the observations of Angevine,¹⁴ which showed that the effect of roentgenotherapy upon experimental streptococcal and staphylococcal skin infections was to increase the size of the lesions, to produce more necrosis and to enhance the invasiveness of the microorganisms.

The definite value of irradiation in gas gangrene has not as yet been proven, and statements such as "The use of roentgen ray in treatment of gas gangrene approaches the action of a specific, in that it is by far the most effective measure so far employed," and "the use of serum is not absolutely essential to recovery and its use should be conservative, avoiding serum sickness, which only adds to the patient's difficulty" are hardly justifiable in the light of available evidence.

Bliss and Long¹⁵ noted that sulfanilamide had a curative effect in peritonitis produced in mice by injection of *Clostridium welchii*. It should be pointed out that the infection of the peritoneum is quite different from that observed in traumatized muscles. Kendrick¹⁶ was unable to demonstrate any marked therapeutic value of neoprontosil, sulfanilamide or sulfapyridine in *Clostridium welchii* infections produced experimentally in the muscles of guinea-pigs. In the treated group, there was a mortality of 89.5 per cent, while in the control group it was 94.3 per cent.

Reed and Orr¹⁷ found, in experimental work on guinea-pigs, that the administration of sulfanilamide, sulfapyridine, sulfamethylthiazole or sulfathiazole showed increasing effectiveness, in the order named, in controlling infec-

tions produced by *Clostridium welchii*, *Clostridium septicum*, *Clostridium sordellii* or *Clostridium novyi*. The best results were obtained when the drug was introduced directly into the wound. However, even in their experiments, it was necessary to introduce the drug before the full development of gas gangrene. Gordon and McLeod¹⁸ also found experimentally that local administration of sulfanilamide drugs was more useful than the oral. However, they also found that sulfanilamide drugs were inferior to antisera in the prophylaxis of gas gangrene.

Sadusk and Manahan¹⁹ demonstrated the bacteriostatic action of sulfanilamide on *Clostridium welchii* *in vitro*. Such action was inversely proportional to the number of organisms used in the inoculum. No bactericidal effect was noted since growth readily took place if organisms, the growth of which had been suppressed by sulfanilamide, were transferred to a sulfanilamide-free medium. They attribute Spray's²⁰ inability to demonstrate bacteriostatic effect of sulfanilamide to the heavy inoculation of *Clostridium welchii* used in his experiments.

Clinically, Bohlman²¹ reported three cures in patients treated with sulfanilamide for gas gangrene developing following compound fracture of the lower extremity. All of Bohlman's patients, however, received some serum. Sadusk and Manahan¹⁹ also reported two cures in postabortal *Clostridium welchii* infections with positive blood cultures. This is of some significance in view of a mortality of 85 per cent in this type of infection in patients receiving no specific therapy and 47 per cent for patients treated with specific antiserum.

Caldwell,¹¹ using the guinea-pig as the experimental animal, produced the counterpart of a compound fracture and infected it with a lethal number of *Clostridium welchii*. Sulfanilamide crystals implanted in such wounds after débridement seldom controlled or prevented the development of gas gangrene. However, the administration of large doses of sulfanilamide by intraperitoneal injection after the wound had been debrided, irrigated and left open, prevented the development of gas gangrene in a high percentage of instances.

Stephenson and Ross²² compared the effectiveness of antiserum and chemotherapy and concluded from their studies that "*Cl. welchii*—Type-A—Sulfanilamide and sulfapyridine protected mice against a small number of lethal doses injected intraperitoneally as suspension of vegetative organisms in sterile soil suspension. Treatment with antitoxic serum was also effective in the case of a strain of high toxigenicity, but failed against a strain of low toxigenicity though probably of higher invasiveness. When the infected soil suspensions were injected intramuscularly, considerably more organisms were necessary to produce a fatal result and the drugs were of value only against a sublethal infection. Serum treatment was better and saved mice even from lethal doses.

"*Cl. septicum*—Sulfanilamide had little influence on infections of mice injected intraperitoneally or intramuscularly with suspensions of sporing

and nonsporing organisms in calcium chloride solution or sterile soil suspension. Sulfapyridine was better, in large doses it saved 50 per cent of the animals. Treatment with a single dose of antitoxic serum was at least as effective as sulfapyridine, but the best results were obtained when sulfapyridine was combined with serum, large doses of the drug being given immediately after infection and serum up to 24 hours later.

"With two strains of *Cl. oedematiens* tested so far it has been shown that neither sulfanilamide nor sulfapyridine has any influence on the course of the infection."

In considering the value of chemotherapy in clinical cases, attention again is directed to the fact that gas gangrene is very rarely a monobacterial infection. It is extremely likely that the effect of chemotherapy in improving the results in clinical cases may be due to its action on the other organisms present. In this connection, it is worth while citing the quotation from the Surgeon-General's report, as quoted by Bohlman²¹: "In Base Hospital No. 15 AEF, in 73 cases of gas gangrene with death, activity of the gas bacilli was self-limiting and practically confined to the first week after the wound was received. There was a drop in anaerobes from 38 to seven per cent during the first seven days, as the common pyogenes streptococcus and staphylococcus accumulated rapidly in the wound. Infections with anaerobes alone showed a high death rate but a short period of danger to life. A streptococcic bacteremia was by far the most important cause of death, especially in patients living beyond the first week, which was roughly established as a self-limiting period of gangrenous process and many deaths attributed to the anaerobes were in reality deaths due to streptococci in the process of replacing them." If a number of these deaths were due to the streptococcus, then the value of chemotherapy clinically could not be questioned.

SUMMARY

It is shown that irradiation has no demonstrable effect on *Clostridium welchii* infection in the pigeon with the dosage of irradiation used. It is shown also that irradiation used in conjunction with serum is a detriment rather than a benefit. Sulfanilamide as used in these experiments was also without value. Serum alone was of value in saving the lives of the majority of the pigeons. It is suggested that the sulfonamides may be of value in controlling the secondary infection so commonly observed in clinical gas gangrene infection.

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BIBLIOGRAPHY

- ¹ Kelly, J. F. X-ray as an Aid in Treatment of Gas Gangrene, *Bacillus Welchii* Infection. Preliminary Report. *Radiology*, 20, 296, April, 1933.
- ² Kelly, J. F., and Dowell, D. A. Present Status of X-ray as Aid in Treatment of Gas Gangrene. *Jour. Amer. Med. Assn.*, 107, 1114, October, 1936.

- ³ Kelly, J F Present Status of X-ray as Aid in Treatment of Gas Gangrene Radiology, 26, 41, January, 1936
- ⁴ Kelly, J F, Dowell, D A, Russum, B C, and Colien, F I Practical and Experimental Aspects of Roentgen Treatment of Bacillus Welchii (Gas Gangrene) and other Gas-Forming Infections Radiology, 31, 608, November, 1938
- ⁵ Kelly, J F, and Dowell, D A Roentgen Treatment of Gas Gangrene Arch Phys Therapy, 20, 88, February, 1939
- ⁶ Kelly, J F, and Dowell, D A Roentgen Treatment of Acute Peritonitis and other Infections with Mobile X-ray Apparatus Radiology, 32, 675, June, 1939
- ⁷ Kelly, J F, and Dowell, D A Roentgen Treatment of Acute Infections with Modified Mobile X-ray Apparatus Including Case Reports U S Navy Med Bull, 37, 600, October, 1939
- ⁸ Elhason, E L, Erb, W H, and Gilbert, P D Clostridium Welchii and Associated Organisms Review and Report of 43 New Cases Surg, Gynec and Obst, 64, 1005, June, 1937
- ⁹ Bull, C G, and Pritchett, I W Toxin and Antitoxin of and Protective Inoculation against Bacillus Welchii Jour Exper Med, 26, 119, 1917
- ¹⁰ Bieter, R N, Baker, H B, Beaton, J G, Shaffer, J M, Seery, T M, and Orr, B H Nervous Injury Produced by Sulfanilamide Jour Amer Med Asso 116, 2231, May 17, 1941
- ¹¹ Caldwell, G A Treatment of Gas Gangrene Experimentally Produced Jour Bone & Joint Surg, 23, 81, January, 1941
- ¹² Caldwell, G A, and Cox, F J Roentgen Ray Treatment of Gas Gangrene ANNALS OF SURGERY, 114, 263, August, 1941
- ¹³ Williams, A J, and Hartzell, H V Gas Gangrene Analysis of 34 Cases Treated in Past Five Years in San Francisco Hospital With Special Reference to Roentgen Ray Therapy Western Jour Surg, 47, 561, October, 1939
- ¹⁴ Angevine, D M Personal communication
- ¹⁵ Bliss, E A, and Long, P H Observations on Mode of Action of Sulfanilamide Jour Amer Med Asso, 109, 1524, November 6, 1937
- ¹⁶ Kendrick, D B, Jr Treatment of Gas Gangrene Infections in Guinea-pigs with Neoprontosil, Sulfanilamide and Sulfapyridine Experimental Study Jour Clin Invest, 18, 593, September, 1939
- ¹⁷ Reed, G B, and Orr, J H Chemotherapy in Experimental Gas Gangrene Lancet, 1, 376, March 22, 1941
- ¹⁸ Gordon, J, and McLeod, J W Relative Value of Sulfonamides and Antisera in Experimental Gas Gangrene Lancet, 1, 407, March 29, 1941
- ¹⁹ Sadusk, J F, Jr, and Manahan, C P Sulfanilamide for Puerperal Infections Due to Clostridium Welchii Jour Amer Med Asso, 113, 14, July, 1939
- ²⁰ Spray, R S Bacteriostatic Action of Prontosil Soluble, Sulfanilamide, and Disulfanilamide on Sporulating Anaerobes Commonly Casually Associated with Gaseous Gangrene Jour Lab and Clin Med, 23, 609, March, 1938
- ²¹ Bohlman, H R Gas Gangrene Treated with Sulfanilamide Report of Three Cases Jour Amer Med Asso, 109, 254, July 24, 1937
- ²² Stephenson, D, and Ross, H E Chemotherapy of Cl Welchii Type-A and Cl Septique Infections in Mice Brit Med Jour, 1, 471, March, 1940

NONINFECTIVE GANGRENE FOLLOWING FRACTURES OF THE LOWER LEG

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GANGRENE aside from that caused by the gas bacillus and other virulent organisms is rare following fractures of the extremities if one is to judge by the meager references to it to be found in the literature. Dodd¹ in 1934 writing on this phase of traumatic surgery, collected a total of 31 cases appearing in the world literature between 1850 and 1934 among which were six cases of fracture of the lower leg followed by gangrene. Since 1934 eight more instances of this complication have been recorded. It is the purpose of this report to describe an additional case and to consider briefly certain germane problems.

Case Report—New York Hospital No. 286442. Male, age 23, was admitted to the New York Hospital within an hour after having been struck by an automobile. He sustained a severe crushing injury of the left lower leg which resulted in a transverse comminuted fracture of the tibia and fibula and chip fractures of the external malleolus and of the talus. There also was an avulsed wound of the soft tissues on the lateral aspect of the foot. On admission the toes were warm and sensation intact, but the enormous hematoma about the foot and ankle precluded palpation of the dorsalis pedis and posterior tibial arteries. The popliteal artery was readily palpated and its pulsation of good volume.

Operation—Under the effect of 120 mg. of novocain crystals injected intraspinally the wound of the lateral aspect of the foot was debrided and covered with a thin split-thickness graft. Steel pins were thrust through the tibia above and below the fractures and anatomic reduction secured by means of a traction-distraction apparatus. The entire extremity was then encased in unpadded plaster splints lightly reinforced with circular plaster bandages.

Subsequent Course—The patient was returned to the ward and the lower extremities elevated at an angle of 45°. Slowly during the course of the next three days his temperature rose to 39° C., pulse 120, and his toes became deeply cyanotic. Gradually cutaneous sensation in the toes was lost. The encasement was removed and the leg placed in a Braun-Boehler splint with traction on the distal pin. The proximal pin which lay well anterior to the anterior tibial artery, was withdrawn. During the course of the next two days the toes, the foot and the ankle became dusky and cool and loss of cutaneous sensation progressed to the level of the lower calf. The calf itself was swollen, tense, and the skin shiny. This state persisted practically unchanged for the next 25 days, though the patient's vital signs returned to normal following the removal of the encasement. On the twenty-seventh day after admission a diagnosis of a large abscess of the muscles of the calf was made. On the basis of this diagnosis a long incision through the skin of the lateral aspect of the lower leg disclosed gangrenous but not infected bundles of muscles. These were smoky-white in appearance, edematous and gelatinous. All of the muscles supplied by the anterior tibial artery, namely the peroneus longus and brevis, extensor digitorum longus, extensor hallucis longus and tibialis anterior, were included in this process. Slowly

these gangrenous muscles separated from surrounding viable structures, the wound became lined with granulation-tissue, and was epithelized by grafts. The tibia united firmly, and the patient was discharged six months after admission, able to walk with the aid of a brace. On discharge the anesthesia of the foot was still present.

The patient has been followed closely since discharge from the hospital, and, one year later, he is actively engaged as an iron worker, though still dependent upon his brace.

The interest in this patient lies not in the fracture but in the complication of noninfective gangrene of an isolated group of muscles. On subjecting this case to careful analysis, two features seem to be of paramount significance: (1) That the nerve supply of the lower leg and foot, which was intact on admis-

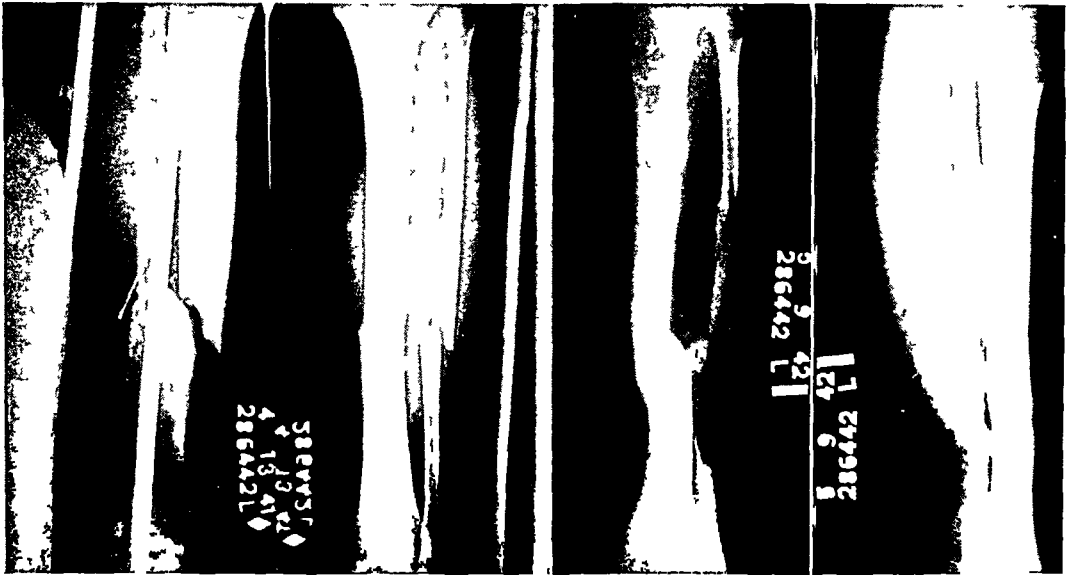


FIG 1—Anteroposterior and lateral roentgenograms of the tibia and fibula taken on admission.

FIG 2—Anteroposterior and lateral roentgenograms of the tibia and fibula taken 12 months after injury.

sion, failed slowly over the course of the next two or three days, and (2) that the blood supply of the foot, which also was normal on admission, early showed signs of embarrassment followed, however, by ultimate survival of the foot. With these facts in mind, it is possible to reconstruct the course of events that led to this untoward complication. As a result of the severe crushing nature of the injury the anterior tibial artery probably was torn sufficiently to damage its intima and a thrombus slowly began to form at the site of the injury. During the course of the next few days the thrombus became so large that it occluded the lumen of this vessel. Directly dependent upon the progressive nature of this lesion are the phenomena noted clinically, namely, the intact nerve and blood supply on admission, their slow failure over the course of a few days as the integrity of the blood supply became compromised, and finally gangrene and complete loss of sensation. The ultimate viability of the foot in all probability may be ascribed to the rich collateral circulation about the ankle joint, and in the foot between the distal branches of the anterior and

posterior tibial arteries, namely, the peroneal, the dorsalis pedis and the fibular and tibial plantar arteries. Obviously, however, though this was abundant, it was inadequate to supply in retrograde fashion the domain of the proximal portion of the anterior tibial.

In an effort to establish further the validity of these assumptions, all of the reported cases of this complication, appearing in the literature from 1850 to the present time, have been critically reviewed (Table I). Analysis of these cases reveals the following interesting facts:

Age Incidence—The average age for this group of 15 cases is 26 years. Because such a large majority of these patients fall into a relatively young age-group, degenerative diseases of the arterial wall can largely be discounted as a factor predisposing their vessels to injury and subsequent occlusion.



FIG. 3—Unretouched photograph of the leg taken while in traction, showing the extent of the incision necessary to evacuate the gangrenous tissues.

Degree of Injury—If the group be divided on the basis of severity of their injury, there are six which may be considered severe, seven moderate, and two mild. Thus, though it is apparent that gangrene as a complication is more frequently associated with the severer types of injury, the two which are classified as mild justify the conclusion that this is not invariably the case. Conversely, it is a matter of common surgical experience to see severe injuries of the lower leg unassociated with this complication.

Site and Extent of Fracture—In the majority of the cases the fractures were extensive and involved both bones of the lower leg. There are, however, two notable exceptions, namely, the one in which the skeletal injury was merely a separation of the superior tibial epiphysis and the one in which only the fibula was broken. The sites of fracture were about evenly distributed between the upper, middle and lower thirds, some were compound, some were oblique, some transverse, and many were comminuted. It seems likely, therefore, that no particular site or type of fracture predisposes especially to this complication.

TABLE I
NONINFECTIVE GANGRENE OF THE LOWER LEG AND FOOT FOLLOWING FRACTURES OF THE TIBIA AND FIBULA—14 CASES

Case No	Author Ref Date	Age	Degree of Trauma	Fracture	E tent	Gangrene	Artery Occluded	Type of Fixation	Treatment and Result
1	Schultz ¹ 1897	32	Moderate	Tibia midthird	Lower leg and foot	1st day	Popliteal		Amputation femur
2	Jungst ¹ 1899	20	Severe	Tibia fibula at upper end	Lower leg and foot	3rd day	Popliteal		Amputation lower third
3	Muir ¹ 1924	36	Mild	Fibula upper third	Foot	4th day	Anterior tibial Posterior tibial	Traction	Amputation lower leg and foot
4	Gregora ¹ 1927	27	Severe	Supramalleolar tibia and fibula	Foot	4th day	Popliteal	No incasement	Amputation lower leg
5	Susam ² (a) 1933	41	Moderate	Popl hematoma Tibia and fibula upper third	Lower leg and foot	Prior to 16th day	Anterior tibial Posterior tibial	Traction	Amputation upper tibia
6	Susam ² (b)	37	Moderate	Tibia and fibula upper half	Lower leg and foot	6th day	Anterior tibial Posterior tibial	Traction	Amputation through fracture
7	Susam ² (c)	23	Moderate	Tibia and fibula lower third	Foot	7th day	Posterior tibial	Traction	Amputation refused
8	Susam ² (d)	11	Severe	Tibia and fibula, upper third	Lower leg and foot	1st day	Anterior tibial Posterior tibial	No incasement	Useless foot Amputation lower thigh
9	Jones ¹ , 1934 (Dodd)	32	Severe	Tibia and fibula, lower half	Lower leg and foot	4th day	Anterior tibial Posterior tibial	Incasement	Amputation lower thigh
10	Dodd ¹ 1934	29	Severe	Tibia and fibula	Lower leg and foot	5th day	Anterior tibial Posterior tibial	Incasement	Amputation upper tibia
11	Curry and Bishop ³ 1937	16	Mild	Separation of superior tibial epiphysis	Lower leg and foot	3rd day	Popliteal	Incasement	Amputation mid thigh
12	Fitte ⁴ (a) 1938	10	Moderate	Supramalleolar tibia and fibula	Foot	4th day	Anterior tibial Posterior tibial	Traction	Amputation lower leg
13	Fitte ⁴ (b)	28	Moderate	Tibia and fibula, lower third	Foot	3rd day	Anterior tibial	Cast	Amputation lower leg
14	Ottolenghi and Spinelli ⁶ 1939	25	Moderate	Tibia and fibula	Lower leg and foot	4th day	Anterior tibial Posterior tibial	Traction	Amputation upper lower leg
Author's case 1942		23	Severe	Tibia and fibula	Anterior and lateral crural M Peroneal M	5th day ²	Anterior tibial	Cast	Function of foot fair

Extent of the Gangrene—In nine cases this involved the lower leg and foot, in five, the foot alone, and in the present case only the lateral muscles of the calf

Artery Occluded—In view of the fact that all but two cases terminated in amputation, an unusual opportunity was afforded to determine accurately from the specimens where the occlusive process was located. In four, this was the popliteal, in eight, both the anterior and posterior tibial arteries were involved, in one, the posterior tibial alone, and in one, the anterior tibial alone. In this last case amputation was not performed but the gangrenous process

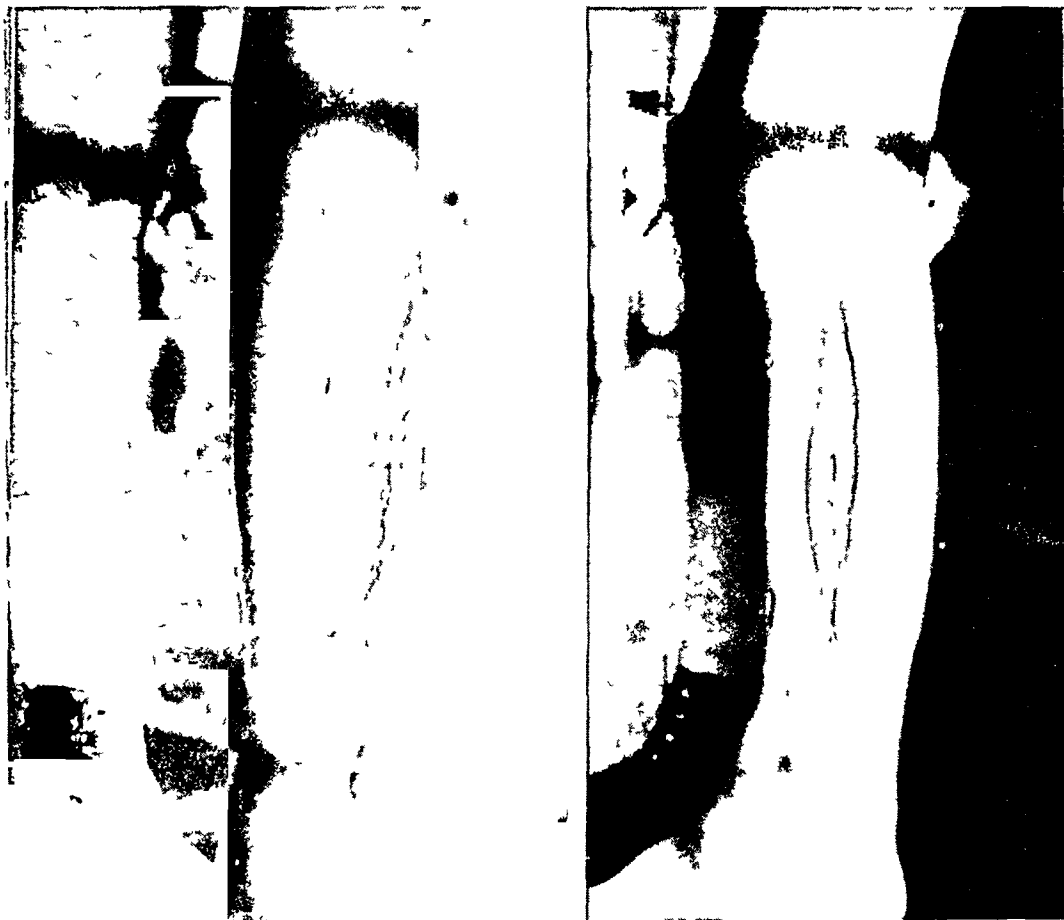


FIG 4—A and B Unretouched photographs of the leg 11 months after injury

corresponded so accurately to the areas receiving their blood supply from the anterior tibial artery that it has been assumed that it was the circulation of this artery which was compromised. There is, of course, a very definite relationship between the artery damaged and the extent of the gangrene. The reasons for vascular damage in these injuries are discussed below.

Method of Treatment of the Fracture—This problem was reviewed with great interest, for during the hospitalization of the patient the opinion was voiced that the encasement might have been the cause of the complication. Although it is impossible to refute this indictment of the encasement, it was found out that of the 13 cases in which data were available, six had been treated with traction, five with encasements, and two, without either of these

aids to fixation. It seems justified, therefore, to postulate that the complication, in all probability, was not related to the method employed for immobilization.

Results—In all but two cases amputation became imperative, five through the thigh and eight through the lower leg. The two exceptions are one case which refused amputation, and was left with a useless leg, and the present case left with a foot functioning only partially even when supplemented by a brace. There were no deaths in this series of cases.

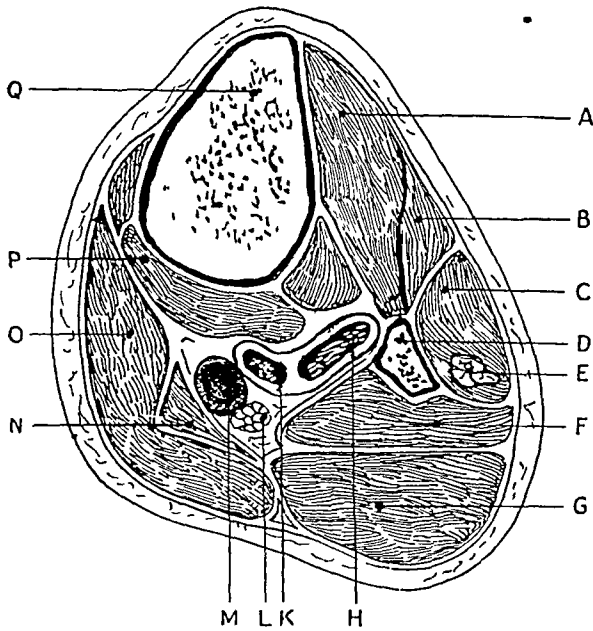


FIG 5—Photographic section through the upper third of the right leg at the level of the bifurcation of the popliteal artery, this is at the origin of the anterior tibial artery, as it arises from the termination of the popliteal artery and runs horizontally forward to the anterior compartment of the leg in close proximity to the fibula.
(Dodd, Harold Brit Jour Surg, 22 246, 1934 35)
(Courtesy British Journal of Surgery)

- Key—
 A Tibialis anticus
 B Extensor digitorum longus
 C Peroneus longus
 D Fibula
 E External popliteal nerve
 F Soleus (fibular head)
 G Gastrocnemius
 H Anterior tibial artery
 K Termination of the popliteal artery and the beginning of the posterior tibial artery
 L Internal popliteal nerve
 M Internal popliteal vein
 N Soleus (tibial head)
 O Gastrocnemius
 P Flexor longus digitorum, with tibialis posticus anterolaterally
 Q Tibia

DISCUSSION—In considering the cases of gangrene following fractures of the lower leg from the point of view of the etiology of the complication, the most important single factor seems to be the damage sustained by the blood vessels of this portion of the lower extremity. Dodd, in his survey of the subject, calls attention to the fact that the bifurcation of the popliteal artery is particularly vulnerable because of its anatomic relationships. He states "This is anchored by the fibrous arch of the soleus, by the passage of the anterior tibial artery over the interosseous membrane, by its proximity to the fibula and by the origins of small anastomotic branches to the knee joint."

For the cross-section through the termination of the popliteal artery I am indebted to Professor Harris, of University College Hospital. He very kindly sectioned a leg, which was photographed, such a diagram is, I think, unobtainable from the textbooks. He pointed out the comparatively intimate association of

the bifurcation with the neck of the fibula. He showed me radiograms demonstrating on the inside of the neck of the fibula a slight groove which is made by the anterior tibial artery as it passes from behind to the front compartment of the leg. This emphasizes the vulnerability of the artery to injury in fractures of this region of the fibula."

In other words, the origins of the anterior and posterior tibial arteries are so rigidly fixed by the surrounding structures that they are subject to injury not only by direct violence, but also by force transmitted to their bifurcation from other parts of the leg. For instance, in Case 3, a fracture of the fibula alone was sufficient so severely to damage both of these vessels that gangrene of the foot occurred. Further, Dodd insists, with real justification, that not only will complete division, penetration or partial rupture of the artery be sufficient to effect occlusion, but also that contusion or rupture of the intima alone will result in occlusion of the vessel with thrombus forming at the site of such intimal damage. He also points out that segmental spasm due to injury may lead to gangrene if allowed to persist for any great length of time. The present case, as well as others recorded, tend to support the claim that any fracture of the lower leg may be associated with damage to the arteries of sufficient severity to impair the circulation to such a degree that the complication of noninfective gangrene occurs.

Treatment —Gangrene, once it has occurred, is amenable to only one therapeutic procedure, namely, amputation. The logical approach to this complication, therefore, is the early recognition of threatened gangrene and the prompt adoption of methods of treatment which might reasonably be expected to prevent its development. If in every case of fracture of the bones of the lower leg the possibility of gangrene were borne in mind, this complication might perhaps be averted. A diagnosis of impending gangrene will not likely be made if it is not considered as a possibility. Particularly should fractures of the lower leg be watched for evidence of failing arterial pulsation, progressive loss of sensation, coldness, increasing cyanosis and pain. Should any one or any combination of the signs or symptoms appear, a progressive thrombotic process must be suspected. Adequate heparinization of the patient should be strongly considered as a method of preventing further thrombosis. A wide incision should be made in the neighborhood of a large hematoma to relieve pressure and to explore for an injured vessel. If possible, such a vessel should be repaired by end-to-end suture and even perhaps by a free venous graft. Some form of sympathetic block must be instituted. A plea is made for the principle of "look and see" rather than "wait and see." Since most of the cases presented an interval of time of from one to sixteen days before gangrene occurred, some warning of the imminence of the complication is given. In the present case the gangrenous process probably did not start until about the third day. If the serious nature of the complication had been anticipated, it is possible that it might have been avoided by the institution of one or more of the measures outlined above.

SUMMARY

All reported cases of noninfective gangrene following fractures of the lower leg have been reviewed and tabulated.

An additional case has been recorded in detail.

The anatomic relationships of the division of the popliteal artery into the

anterior and posterior tibial arteries have been found to be the predisposing factors in this complication

Methods of diagnosis and treatment of impending gangrene have been suggested, in order to prevent this process from reaching an irreversible end-point

REFERENCES

- ¹ Dodd, Harold Gangrene Following Fractures (Excluding Gas Gangrene) Brit Jour of Surg, **22**, 246, 1934-35
- ² von Susani, O Uber Beimgangran bei Unterschenkelbruchen Deutsche Zeitschrift f Chirurgie, **240**, 771, 1933
- ³ Curry, G J, and Bishop, D L Diastasis of the Superior Tibia Complicated by Gangrene Jour Bone and Joint Surg, **19**, 1093, 1937
- ⁴ Fitte, Marcilo Gangrene of the Foot Due to Supramalleolar Fractures Prensa med Argent, **25**, 194, 1938
- ⁵ Fitte, Marcilo Traumatic Gangrene Due to Closed Fractures of Extremities Bol y trab Soc de cir de Buenos Aires, **23**, 508, 1939
- ⁶ Ottolenghi C E, and Spinelli, C A Grave Vascular Complications of Closed Fractures Rev ortop y traumatol, **9**, 90, 1939

RECURRENT ULCERATION FOLLOWING SUBTOTAL GASTRECTOMY IN THE TREATMENT OF GASTRODUODENAL ULCER*

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ALTHOUGH subtotal gastrectomy has been employed in the treatment of gastroduodenal ulcer for more than two decades, it has not been possible, as yet, to discuss its asserted effects upon an adequate factual basis. The usefulness of the operation has been ascribed to its efficacy in preventing the faults of more conservative measures, particularly those of gastro-enterostomy. Specifically, the proponents of subtotal gastrectomy have claimed that its radical approach not only minimizes the incidence, but also averts the serious complications of subsequent ulceration. Up until now, attention has been principally focused upon the first of these contentions. Despite ceaseless debate and discussion, no agreement exists concerning the frequency of renewed ulceration following other operations. Moreover, as patients have been observed to develop recurrent symptoms after remaining well for periods as long as 30 years, it has become increasingly evident that any contention as regards a therapy's efficacy to prevent reactivations of the disease can carry little weight, unless it is supported by the results observed in the following of cases over extended periods of time. Unfortunately, no method has as yet been devised for determining how long patients must be observed to permit conclusive inferences on that score. Time and experience have proved that the commonly employed standard of a five-year follow-up is insufficient, at least for evaluating the results of any therapy for duodenal ulcer, and there is much doubt concerning the validity of conclusions based upon ten-year studies. Up to date, there have been few reports, if any, with the employment of subtotal gastrectomy which fulfill these questionable criteria. Its complicating incidence of recurrent ulceration, therefore, awaits the results of further experience and the development of a satisfactory method for appraising them.

The second claim made for subtotal gastrectomy relates to its efficacy in averting the serious complications of peptic ulcer. Although this contention lends itself to more definitive discussion, it has received relatively little critical consideration. This has been due, in part, to the limited opportunity to study the operation's late effects. In view of these facts, it was thought that it might be of value to report and discuss the clinical features of the cases that are known to have developed symptoms and evidence of recurrent ulceration.

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after the employment of subtotal gastrectomy for duodenal and gastric ulcer in the Gastric Clinic of Mount Sinai Hospital, New York, N. Y. These cases, which have been detected in following a significant number of patients for varying lengths of time during the past 17 years, contribute a factual perspective to an aspect of the operation, which, thus far, has been so speculative.

In recent years the status of some of the problems requiring consideration in discussing the data of this report has changed so materially that it is necessary, for purposes of clarity, to indicate the particular point of view that is held concerning them. In the first place, there has been much confusion as to what is meant by subtotal gastrectomy. While different interpretations have been given to the rôle which certain factors play in contributing to its success, *e g*, extent of resection, method of restoring continuity, removal of lesion, *etc*, it is well agreed that the basic prerequisites of the operation are the removal of the pylorus, a radical resection of all antral tissue, and the excision of the ulcer. Since operations involving limited resections, *e g* pylorotomy or the prepyloric exclusion, which retains the pylorus itself, do not fulfill these prerequisites, cases of those categories were not included in this report. Likewise, operations that employ entero-anastomoses were omitted, since that procedure tends to divert the alkaline intestinal contents and thereby to defeat a major objective of subtotal gastrectomy—the influencing of the gastric acidity. The required extent of resection is not easy to define. This clinic has employed a technic, originally devised by A. A. Berg,¹ in which the proximal level of resection reaches well above the reentrant angle of the stomach, gastro-intestinal continuity being restored by a partial terminal-lateral anastomosis (Hofmeister method). Until three years ago the retrocolic anastomosis was preferred, so that the results in this report relate particularly to that method.

The employment of subtotal gastrectomy has been so closely linked with the problem of gastrojejunal ulceration, that the principal interest in any report of its results centers about that question. A consideration of its significance is particularly pertinent to the purposes of this discussion. Gastrojejunal ulceration is generally regarded to be an induced condition, which results from the anastomosing of the jejunum to the stomach. While primary ulcers of the jejunum have been reported, they are so rare that, for all intent and purposes, they may be considered nonexistent. Various theories have been suggested for the causation of anastomotic ulcer, but none have proven adequate, since it has been found to occur after every suggested technic and despite every precaution. While it may follow any operation which joins the stomach to the jejunum, it is observed almost exclusively in ulcer disease, and only in the presence of free hydrochloric acid. This communication agrees with the current opinion which considers gastrojejunal ulcer to be caused by the factors essentially responsible for ulcer disease itself, and that it is, therefore, a recurrent peptic ulceration. As such, its effects are no different from those seen with an ulcer of the stomach or duodenum, *e g*, pain, hemorrhage, perforation, obstruction, *etc*. It is because of anatomic

factors that the complications resulting from the activity of anastomotic ulceration tend to be more serious and more difficult to treat

Inasmuch as this report represents the experience of a particular clinic, certain factors relevant to it must be appreciated. In the first place, it relates to patients who had been operated upon between 1923 and January 1, 1940 on the Gastric Ward Service of Mount Sinai Hospital, New York, N. Y. The results reflect the experience of an entire staff of trained gastric surgeons rather than any one individual surgeon. The patients were preponderantly Jewish, and were chiefly factory workers and tradesmen. There were relatively few artisans and clerical workers, and practically no agricultural workers. The indications for operation were, as a rule, failure to respond to adequate medical treatment, *e g*, intractable pain, unrelieved obstruction, and repeated hemorrhage. The cases, comprising this study were observed in the regular Follow-up Clinic, which is conducted bimonthly before a group of surgeons, gastro-enterologists, and house staff. All observations are made through personal interviews, and are the result of a combined rather than an individual opinion.

The symptomatology, pathology and diagnostic features of recurrent ulceration, which in our opinion includes gastrojejunal ulcer, have been fully described in numerous reports and need no special consideration. The term "ulcer" and "ulceration" are used interchangeably as descriptive of the "peptic ulcer" in the pathologic sense. It is frequently difficult and often impossible, clinically, to determine the exact cause of complaints after gastric operations. Although roentgenologic investigation reveals accurate confirmatory evidence of recurrent ulceration in a high percentage of examinations, there are instances in which the findings are negative. These cases cannot be differentiated with certainty from those with "gastritis" or "erosions," which give rise to epigastric pain and bleeding. This study, therefore, has been limited to those patients with complaints after subtotal gastrectomy, who had manifested unequivocal or convincing presumptive evidence of recurrent ulceration. This evidence will be discussed presently.

While, surgically, a recurrence of the disease is the most important cause of failure after radical resection, it must be remembered there are other factors which may contribute to an unsatisfactory result. For example, about 10 per cent of the patients manifested a train of symptoms, which seemed to be caused by some disturbance in physiology, resulting from the operation itself rather than any activity of ulcer disease. Some had symptoms of a vagotonic type, *e g*, sweating, nausea, palpitation, weakness, others complained of failure to gain weight, and a small number suffered from periodic diarrhea. While these symptoms were disturbing, for the most part, they were not incapacitating. There was another group of ten patients with so-called dyspeptic complaints, *e g*, heart burn, sour eructations, who contended they were not improved by the operation. Repeated examinations have failed to reveal any organic cause for their complaints, and they, unquestionably, represent a neurotic group, such as is encountered in every field of surgery.

TABLE I
SUBTOTAL GASTRECTOMIES (1923-1940)

Type of Case	Operative Survivors	Recurrences	Basis for Diagnosis		
			Operation	Gastroscope X-ray	Gross Bleeding
I Duodenal Ulcer					
(a) Primary*	366	27	6	16	5
(b) Secondary†	136	13	7	4	2
(c) Total	502	40	13	20	7
II Gastric Ulcer	98	1	0	1	0

* Primary case—no previous gastric operation

† Secondary case—one or more previous gastric operations

A summary of the data, upon which this study is based, is given in Table I. It will be noted that 41 cases are classified as recurrent ulcerations. The diagnosis was definitively established by operation* or by autopsy in 13 cases. In 21 of the remaining 28 the diagnosis was confirmed roentgenologically or gastroscopically. There were seven patients who returned with severe, painless, gross hemorrhage (melena or hematemesis) at intervals varying from a few months to several years after operation. Although the roentgenologic examinations in these cases were negative, it is not unlikely that recurrent ulcerations were responsible for their bleeding. There are well-founded reasons for such an assumption. In the first place, we know from our experiences with the employment of subtotal gastrectomy in cases of "painless bleeding" following gastro-enterostomy, that the resected specimens frequently reveal healed or superficially healing gastrojejunal ulcerations.² In the majority of these instances, the roentgenologic examinations are negative, but it must be borne in mind that investigative examinations and surgery are usually carried out after cessation of the bleeding and after prolonged medical treatment. It is not usual to observe similar roentgenologic and pathologic findings in cases of primary duodenal ulcer associated with otherwise symptomless bleeding after comparable preoperative treatment. Moreover, there have been several patients in this clinic in whom operation had been limited merely to exploration because of the paucity of findings. At subsequent celiotomy, because of recurrent symptoms, large active duodenal ulcers were found. There is no doubt, therefore, that a peptic ulcer may give rise to painless hemorrhage, and that negative roentgenologic findings do not controvert that diagnosis. This presumptive evidence of recurrent ulcer must be weighed against the possibility of erosions and postoperative gastritis as causes for painless bleeding. This aspect of that problem has been fully considered by Moschowitz, Mage and Kugel.³ There is a well-recognized school which regards erosions and gastritis to be manifestations of ulcer disease, particularly when

* Operative findings indicating active or healed ulcers were regarded to be adequate evidence of such lesions. In two instances penetrating jejunal ulcers were encountered, but not removed, so that specimens were not available for examination. In nine cases specimens were available. Seven disclosed ulcers. No evidenced ulceration was found in two, in which the surgical findings were considered to be those of healed lesions.

they occur in individuals who are known to have had peptic ulcer. In a sense, it seems to be an academic question, whether a severe hemorrhage, occurring months or years after subtotal gastrectomy, arises from an ulcer or an erosion. In the final analysis, the operation did not protect the patient against a serious complication of ulcer activity.

There were four patients who returned with recurrent symptoms at intervals of six months, two, six and seven years after their operations. Their roentgenologic examinations disclosed small, tender pockets, which appeared to be in the stomach proper, near the stoma, and in the region of the lesser curvature. One of these cases was the only recurrence detected after subtotal gastrectomy for gastric ulcer, in this clinic during the past 17 years. The patient was a male, age 58, who was subjected to operation after one year of severe postprandial pain. The resected specimen revealed a small lesser curvature ulcer and a severe chronic gastritis. Within six months there was a return of epigastric pain and vomiting. Roentgenograms revealed a small, irregular penetration, suggesting a lesion in the postoperative stomach. This patient was lost to observation after 18 months, but during that time he had several recrudescences of pain and vomiting. The other three cases represent the development of gastric ulcers after the employment of subtotal gastrectomy for the treatment of duodenal ulcer. A newly formed ulcer of the lesser curvature of the stomach is not an infrequent cause for failure after the performance of a gastro-enterostomy for an ulcer of the duodenum. In the remaining 37 cases in this group, the diagnosis of a gastrojejunal ulcer was established, definitively, by operation, roentgenologic and gastroscopic examination in 30 patients, and, presumptively, by the occurrence of "gross hemorrhage" in seven. In view of the solitary recurrence after gastric ulcer, this study resolves itself into a discussion of 40 failures following the employment of subtotal gastrectomy for primary and secondary duodenal ulceration.

There were 44 female patients who survived a subtotal gastrectomy for primary or secondary duodenal ulcer, of these, two are known to have developed gastrojejunal ulcers. One case was of particular interest, in that she developed her first symptoms at the age of 60. After eight months of ineffectual medical therapy, she was subjected to a radical resection, for a penetrating ulcer of the duodenum. Within three months there were severe recurrent symptoms which remained intractable to conservative measures, and necessitated reoperation within a year. At exploration, a large perforating jejunal ulcer was found. The second case was a young woman, age 19, who had experienced ulcer symptoms, including hemorrhage, for three years. Four years following her subtotal gastrectomy she returned with an alarming gross hemorrhage, which had reduced her hemoglobin to 25 per cent. It is asserted that gastrojejunal ulcer rarely occurs in the female, and when it does, it appears late in life. It is interesting that one of these patients was among the most severe, and the other was among the youngest in this whole group of failures.

TABLE II

TIME OF ONSET OF POSTOPERATIVE RECURRENCE

Years Postop	Primary and Secondary Duodenal Ulcer			Gastric Ulcer		
	Surviving Cases	Followed Cases	Recurrences	Surviving Cases	Followed Cases	Recurrences
1 yr	502	453	15	98	95	1
2 yrs	465	385	9	95	82	—
3 yrs	421	330	6	87	69	—
4 yrs	411	280	4	79	56	—
5 yrs	397	250	0	76	52	—
6 yrs	382	218	1	72	45	—
7 yrs	364	211	2	64	39	—
8 yrs	339	179	0	58	34	—
9 yrs	315	152	0	54	34	—
10 yrs	274	128	2	54	31	—
11 yrs	249	113	0	49	26	—
12 yrs	220	97	1	40	17	—
13 yrs	174	75	0	29	11	—
14 yrs	137	53	0	20	7	—
15 yrs	86	33	0	15	6	—
16 yrs	58	21	0	4	2	—
17 yrs	17	8	0			

Time of Onset of Recurrent Symptoms—Table II indicates the number of surviving cases that potentially might have been followed for each of the 17 years of observation, the number of patients that actually was followed, and the postoperative year in which the various recurrences were detected. It will be noted that the renewed ulcerations occurred at intervals varying from less than a year to 12 years after operation. The fact that six of the 40 failures developed after the fifth postoperative year, serves to emphasize the inadequacy of a "five-year" follow-up for appraising results following the employment of subtotal gastrectomy for duodenal ulcer. These late recurrences, moreover, were observed during the period when an increasing percentage of patients became lost to follow-up observation. The meaninglessness of publishing "three- or five-year 'cures' for gastro-enterostomy" was strikingly demonstrated by St. John, *et al*,⁴ in their recent study of results of treatment for peptic ulcer. The above observations are of particular significance since they not only illustrate the uncertainty of cure, but they also emphasize the absolute need for following patients indefinitely, in order to evaluate properly the efficacy of any ulcer therapy.

Symptoms—The symptomatology in this group of recurrences was not essentially different from that observed with primary peptic ulcer, except for their greater severity and intractability. In 23 cases, pain was the only symptom, in six instances the pain was associated with bleeding, and in 12 patients there was gross hemorrhage (melena or hematemesis) with little or no pain. The clinical courses of these patients have been variable. The symptoms became severe enough to necessitate reoperation in 12 patients, ten in this institution and two elsewhere. All these operated cases were found to have gastrojejunal ulcerations. In two instances, the cicatrizing effects of the lesion had caused low-grade partial obstruction, in two other cases, the edema and swelling resulting from active penetration into the adjacent mesen-

teity of the small intestine had produced more acute obstructive symptoms. In one instance, there was a free perforation of a jejunal ulcer, which necessitated an immediate operation. Another patient (unoperated) died from the effects of a gastrojejunal fistula, which was confirmed by autopsy. There are three patients under observation at present, who have been readmitted to the hospital three, five, and nine times, respectively, during the past six years, because of the severity of their complaints. Except for the patients with painless bleeding, who have responded satisfactorily to conservative treatment, the remaining cases have been controlled only with fair success by similar measures.

Hemorrhage—Gross bleeding (melena or hematemesis) was a prominent and serious occurrence in 18 of this group of 41 recurrent ulcerations. The full details of these cases and their implications have been discussed in a previous communication by Colp and the author.⁵ These hemorrhages occurred at intervals of a few months to 12 years after operation, and varied from a moderate to a severe degree. Ten of these patients bled prior to their subtotal gastrectomies, six had repeated episodes. Five of these six patients with multiple hemorrhages also bled several times after operation. There were six cases in which the bleeding was associated with pain, all were found to have jejunal ulcerations, two by operation, and four by roentgenographic evidence. There were 12 cases in which bleeding was the only symptom. All these patients responded to medical therapy. Roentgenologic examinations, made after bleeding had stopped, were negative in seven instances, in three, jejunal ulcers were reported, and in two, lesser curvature defects were noted.

These observations are somewhat at variance with the general impression which exists concerning the particular efficacy of subtotal gastrectomy in the problem of bleeding. The fact that a majority of patients who bled after operation also bled prior to it, may suggest the possibility of a bleeding diathesis. However, it seems far more likely, from the character and history of the clinical material, that the hemorrhages were merely the results of recurring ulcerations or "erosions." While subtotal gastrectomy may not provide a certain assurance against subsequent bleeding, it finds its particular field of usefulness in the problem of the actively bleeding ulcer, because its radical approach entails a direct attack on the lesion. As a consequence, it is far more likely to succeed than is the indirect approach of gastro-enterostomy. However, once the bleeding of a duodenal ulcer is arrested, whether it be by the conservative or the radical operation, a subsequent hemorrhage at a late interval is, as a rule, caused by a gastrojejunal ulceration and not by the original lesion. It is well to remember that this holds true for a gastro-enterostomy performed for duodenal ulcer in its nonbleeding stage.

In reviewing this series of 41 recurrences after subtotal gastrectomy, certain facts stand out clearly. In the first place, there is the striking difference in response of gastric and duodenal ulcer to the same operation. The reason for this difference remains unsolved, and its answer may contribute much

to a better understanding of the ulcer problem. The second significant observation pertains to the question of the relationship between gastric acidity and recurrent ulceration. Up to date, this clinic has not observed a recurrent ulcer in the absence of free hydrochloric acid. Acidity studies⁶ have revealed that subtotal gastrectomy creates an achlorhydria in at least 90 per cent of patients with gastric ulcer, and it produces an apparent achlorhydria in about 50 per cent of patients with duodenal ulcer. It is in this group with unneutralized free hydrochloric acid, that renewed ulceration is encountered. It is to be noted that the observations relating to acidity and those pertaining to recurrent ulceration after radical resection for duodenal and gastric ulcer are closely correlated. These facts not only emphasize that the effect of radical resection to a large extent is due to a modification of the acid factor in gastric digestion, but they also lend much weight to the concept which postulates that an achlorhydria is the best assurance against subsequent ulceration.

Most proponents of subtotal gastrectomy regard the creation of an innocuous achlorhydria to be one of the principal objectives of the operation. Some have contended that if such an effect is not obtained, or if recurrent ulceration develops, it is presumptive evidence of the inadequacy of the extent of resection. Such a doubt naturally arises with every unsuccessful case. However, it must be remembered that as long as any stomach tissue containing parietal cells remains, free hydrochloric acid may be secreted. Experience has shown this to be so. There are certain cases, of which there were two in this series, that continue to have free hydrochloric acid in their gastric contents, in spite of repeated resections which leaves but a minimum of stomach. Some of these patients, presumably, possess an ulcer diathesis that is so severe that ulceration recurs, despite every effort to prevent it. While radical resection is essential, it is not the deciding factor which determines either a gastric achlorhydria or the prevention of renewed ulceration. The difference in response of gastric and duodenal ulcer to the same extent of resection is evidence of that fact.

Recently, certain observers have stressed the removal of the ulcer as a "*sine qua non*" for insuring the success of subtotal gastrectomy. It is interesting to note that 30 of the 41 resected specimens contained the ulcer, so that in this particular experience the excision of the lesion did not safeguard patients against subsequent failure.

It is evident from the manifestations of this group of recurrent ulcerations, *e g*, uncertainty of occurrence, intractability of pain, perforation, repeated hemorrhage, and gastrojejunal fistula, that a patient who is subjected to subtotal gastrectomy is not rendered immune to the serious complications which are noted after other gastric operations. While the likelihood of such occurrences appears to be negligible after its employment for a lesser curvature ulcer of the stomach, it is not insignificant in the case of duodenal ulcer. This failure of subtotal gastrectomy to fulfill completely its anticipated effects in the surgical treatment of duodenal ulcer, does not, itself, negate contentions

as regards its relative merits. This clinic regards radical resection to be the best available operation for duodenal ulcer, but it is the present impression that it leaves much to be desired. At the outset of this report, we indicated the impossibility of drawing logical statistical conclusions concerning the incidence of recurrence under prevailing conditions. To do so is only to create new fallacies and to perpetuate old ones. In our opinion⁷ the statistical confusion which exists concerning the effects of various treatments for peptic ulcer cannot be settled until some generally accepted logical method is devised for studying results in a uniform way, and with a particular provision for the manifold variables which make for unwarranted actual and comparative inferences. It will be noted that, in Table III, the minimal known percentage-incidence of recurrence is recorded. It was determined by computing the known number of recurrences against the total number of surviving patients, and merely means that, in the experience of this particular clinic with the employment of subtotal gastrectomy, the percentage-incidence of recurrent ulceration cannot be less, but may be more than the indicated figures. These results do not permit any valid comparative inferences. To utilize them for such purposes would be misleading.

TABLE III
MINIMAL INCIDENCE OF RECURRENCE

Type of Case	Operative Survivors	Recurrences (Operation + X-Ray)	Recurrences + Gross Bleedings
I Duodenal Ulcer			
(a) Primary Cases	366	22 (6%)	27 (7.4%)
(b) Secondary	136	11 (8%)	13 (9.6%)
(c) Total	502	33 (6.6%)	40 (8%)
II Gastric Ulcer	98	1 (1%)	1 (1%)

SUMMARY

In this communication certain observations have been presented which tend to shed a significant factual light upon the effects of subtotal gastrectomy in the treatment of duodenal and gastric ulcer. There has been no intention to support or refute any contentious point of view, but an attempt has been made to draw attention to certain facts, which may contribute to a better understanding of the *modus operandi* of subtotal gastrectomy, and the nature of its complications.

REFERENCES

- ¹ Berg, A. A. ANNALS OF SURGERY, 92, 340, September, 1930.
- ² Ginzburg, L., and Mage, S. Surg., Gynec., and Obstet., 67, 788-795, December, 1938.
- ³ Moschcowitz, E., Mage, S., and Kugel, V. Am Jour Med Sci., 209, No. 1, 52-59, July, 1941.
- ⁴ St. John, F. B., Harvey, H. D., Gius, J. A., and Goodman, E. N. ANNALS OF SURGERY, 109, 193-218, January, 1939.
- ⁵ Mage, S., and Colp, R. New York State Jour Med., 41, No. 24, 2415-2418, December 15, 1941.
- ⁶ Winkelstein, A. Tr. Am. Gastro-Enterol. Assn., 1933.
- ⁷ Mage, S. Jour Mount Sinai Hosp., 4, No. 6, 1059-1065, March-April, 1938.

PRIMARY CARCINOMA OF THE DUODENUM

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PRIMARY CARCINOMA OF THE DUODENUM is a very rare condition, having a reported incidence of from 03 to 003 per cent of all autopsies, or, in other words, from one case in 3,000 to one in 31,000 autopsies^{16, 21, 27, 31} While an extensive literature has accumulated on this subject, critical analysis of the cases reported demands that many, especially among the earlier papers, must be discarded for the lack of pathologic proof of the diagnosis We wish to present a proven case of primary carcinoma of the third (infrapapillary) portion of the duodenum, and to briefly review the literature in order to emphasize the more important clinical facts and to bring up to date the statistics relative to the incidence and the results of surgical therapy

Case Report—Hosp No 243817 H B, white, male, age 53, was admitted to the Jewish Hospital, August 14, 1941, with pain in the entire right side of the abdomen for 3 mos, radiating to the back, occasionally relieved by food, constipation 6 mos, weakness and anorexia, 3 mos, loss of 20 lbs in 3 mos The pertinent physical findings were pallor, evidence of recent weight-loss, tenderness in the right loin, right lower quadrant, and right costovertebral angle All laboratory data were normal except for a RBC count of 3,860,000, Hb of 56 per cent, and occult blood in the stool Roentgenograms of heart, lungs, and kidneys were normal, a shadow on a plain film of the abdomen was suspicious of gallstones GI series revealed an irregular duodenal cap on most films, judged to be spastic Barium enema showed some irregularity of the cecum Gastrosocopy, 8/24/41, was negative *Preoperative Diagnosis* Malignancy of the cecum and cholelithiasis

Celiotomy, September 5, 1941, revealed a generalized abdominal carcinomatosis, but no intrinsic lesion was observed in any organ Infiltrated para-aortic nodes were palpated all the way up to the root of the mesentery The gallbladder contained calculi An omental nodule, removed for biopsy, was reported as metastatic adenocarcinoma, origin unknown The subsequent course was uneventful until September 18, 1941, the 12th postoperative day, when, while out of bed, the patient complained of sudden severe generalized distress, and died within five minutes The clinical impression of the cause of death was coronary occlusion

Necropsy—No 41-168 Dr I Roy Gold The principal findings were generalized arteriosclerosis, with a fresh coronary thrombosis, carcinoma of the infrapapillary portion of the duodenum, with metastases to the lymph nodes, pancreas, liver, mesentery and peritoneum, cholelithiasis, urolithiasis (bladder), and a small leiomyoma of the stomach wall The duodenal neoplasm (Figs 1 and 2) almost completely encircled the bowel, beginning 15 cm beyond the opening of the common bile duct (which in this case was separate from and 2 cm distal to the opening of the duct of Wirsung), and extended caudad for 6 cm The mucosa in the base of the lesion was excavated in a Y-shaped area but was intact over its raised, firm, pearly-white edges Both ducts and the papilla were entirely uninvolved, and the head of the pancreas was secondarily invaded Posteriorly, the lesion was continuous with a large mass of similar tumor tissue which replaced the para-aortic lymph nodes The microscopic appearance was typical of cylindrical cell carcinoma of intestinal origin (Fig 3)

COMMENT —While the diagnosis of gastro-intestinal malignancy was made in this case before operation, its duodenal origin was not determined either clinically or roentgenographically, or even at exploration. Similar errors are common among reported cases, for several reasons. The symptoms are often vague or obscure, and, as in this case, fail to point to any specific level. When signs of intestinal obstruction are present, the condition is usually mistaken for ulcer or gastric neoplasm, while jaundiced cases are commonly

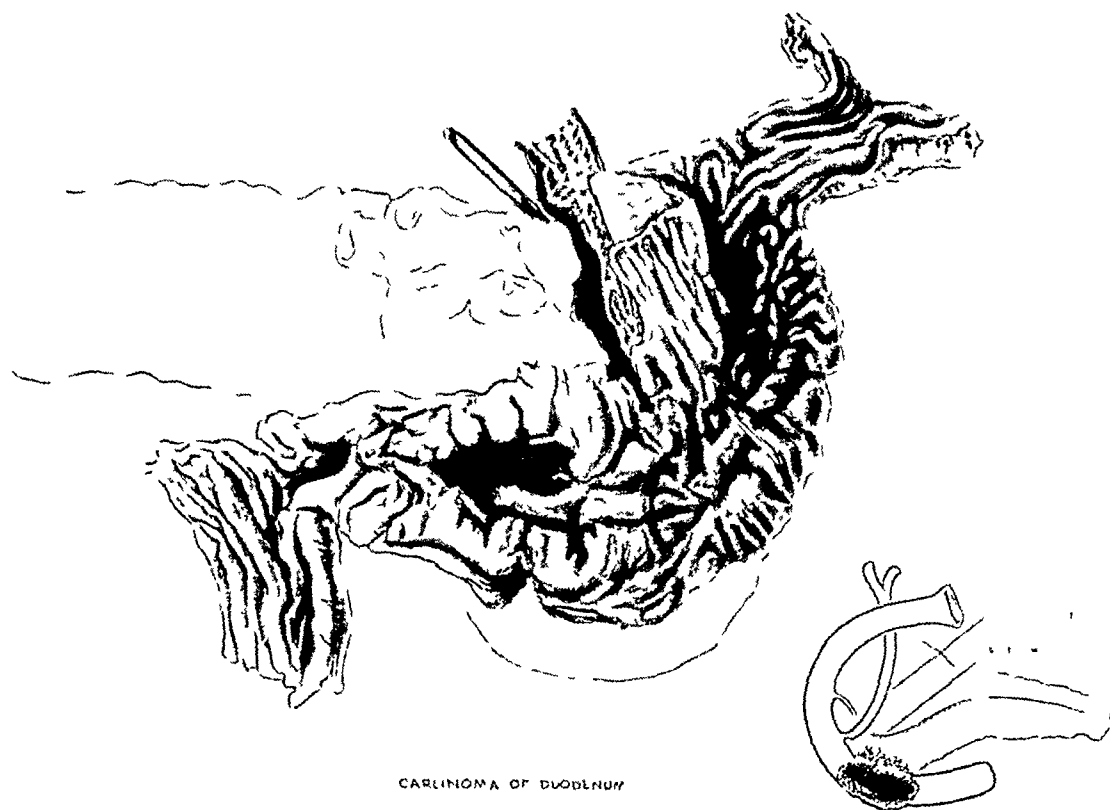


FIG. 1 —Drawing of the gross specimen as opened from behind. Probe is in the opening of the duct of Wirsung, which did not join the papilla of Vater in this case. The common duct and papilla have been opened, the latter appears midway between the duct of Wirsung and the upper margin of the tumor. Inset shows the lesion and ducts in their anatomic positions.

mistaken for carcinoma of the head of the pancreas or for intrinsic common duct obstruction. The location of the primary site at operation may be difficult in the distal retroperitoneal duodenum, as in the present case, where the cancer, though large, was obscured by the massive retroperitoneal lymph node involvement around it as well as by the root of the mesentery.

However, the chief reason for error is the fact that duodenal carcinoma, because of its rarity, is usually not consciously considered. In this case the lesion was plainly to be seen on the roentgenograms, when they were reviewed, to be in the distal duodenum (Fig. 4). The roentgenographic appearance of the condition has been well described by Hoffman and Pack,²¹ Howes,²³ Doub and Jones,¹⁴ and Weintraub and Tuggle.⁴⁷

Primary duodenal carcinoma is anatomically subdivided into suprapapillary, peripapillary and infrapapillary tumors on embryologic, patho-

logic, as well as upon clinical grounds. The suprapapillary portion is above the common duct opening into the duodenum, it is derived from the foregut. The infrapapillary portion arises from the midgut (yolk sac) while the region of the papilla is in the zone between the two. In the latter area, carcinoma may arise from one of several of the epithelia in the region (duodenum, ampulla of Vater, terminal bile duct, or terminal pancreatic duct), while in the other areas, the duodenal mucosa is the sole offending epithelium.

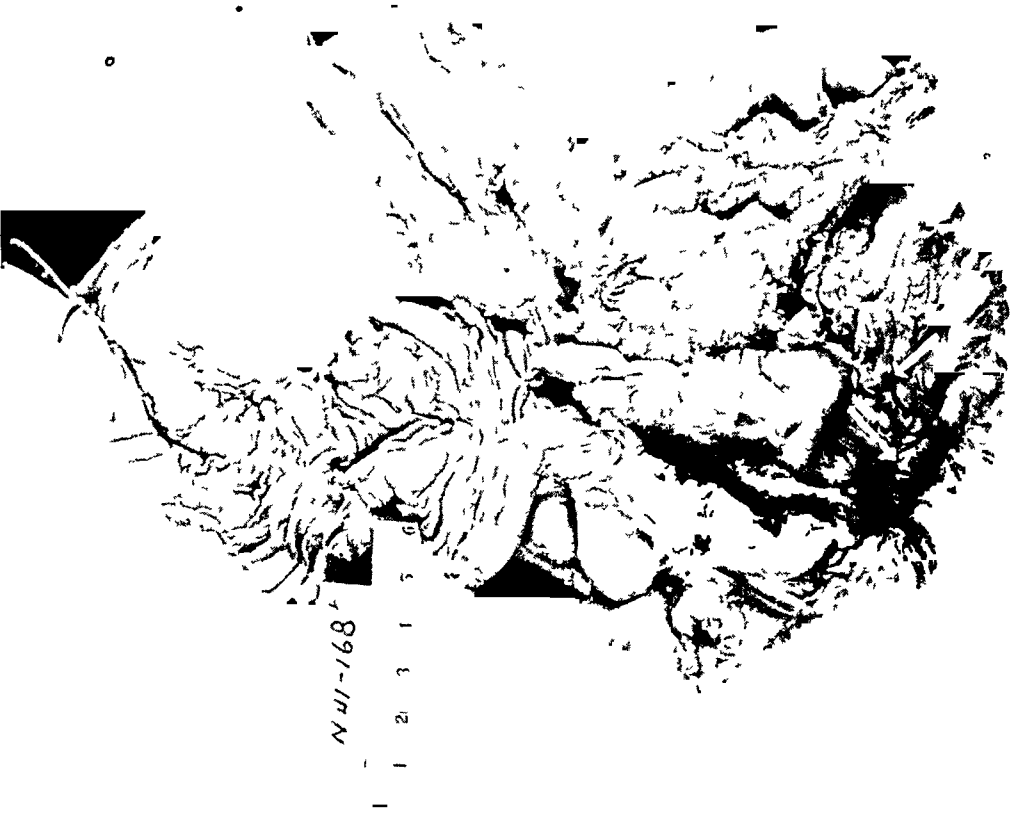


FIG. 2.—Photograph of gross specimen as opened from behind. Upper arrow points to opening of duct of Wirsung, lower arrow to papilla of common duct. The lesion is surrounded by enlarged, invaded retroperitoneal lymph nodes, and above, by the pancreas, also secondarily invaded.

Symptomatology and surgical therapy also vary with the different locations.

The literature of all three groups was very carefully analyzed in a series of three articles by Stewart and Lieber,⁴⁵ and Lieber, Stewart and Lund,^{30, 31} up to 1937, for supra- and infrapapillary growths, and, up to 1939, for peripapillary tumors. These three papers reviewed a total of 565 previously reported cases, of which only 298 were acceptable as authentically proven, to which the authors added 25 of their own, making a total of 323 acceptable cases. We have found 80 additional cases in the literature to date, of which 62 were acceptable. This number, plus the present case, added to the above figure aggregates 386 known proven cases to date.

Of these, 77, or 19.9 per cent, were suprapapillary, 250, or 65 per cent, were peripapillary, and 58, or 15 per cent were intrapapillary. The distribution of the three types, as reported by other authors from smaller series, varied somewhat, but not radically from our figures^{14, 21, 48}

While the over-all incidence of primary duodenal carcinoma, as mentioned above, is from .03 to .003 per cent, Hoffman and Pack²¹ estimated that it comprises .03 per cent of all intestinal carcinomata. They also report that in a series of 228 reported cases of small intestinal carcinoma, 45.6 per cent occurred in the duodenum. Most cases occur in the sixth decade of

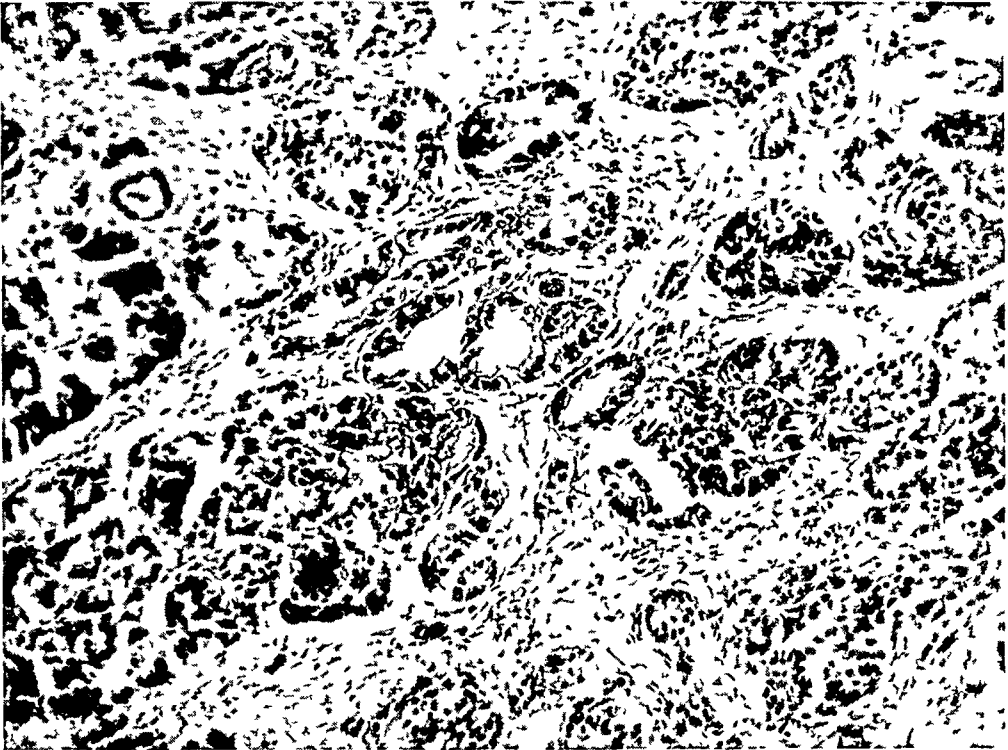


FIG. 3.—Photomicrograph of the general histologic picture. The cells are irregular in size and shape and are arranged in acinar fashion, they invade the muscles and lymphatics of the duodenal wall. (× 200)

life. In the larger series reported, males predominated over females, in ratios varying from 2:1 to 4:1.^{21, 30, 31, 45}

In the review below, certain clinical highlights of the disease are stressed, especially the more recent contributions. For detailed analyses of all phases of the subject, the reader is referred to the excellent articles of Stewart and Lieber,⁴⁵ Lieber, Stewart and Lund,^{30, 31} Hoffman and Pack,²¹ and Cooper.¹²

CARCINOMA OF THE SUPRAPAPILLARY PORTION

Stewart and Lieber⁴⁵ analyzed 104 reported cases, accepted 57 as authentic, and added six of their own, making a total of 63 proven cases up to 1937. We have analyzed 15 additional cases, 14 of which are acceptable, bringing the present total of proven cases up to 77. The new cases are: Three reported by Hoffman and Pack,²¹ two by Cace,⁹ and one each by Jerrel,²⁵ Woods,⁴⁸ Allen,¹ Hart Hansen,²⁰ Nicolini,³⁹ Bolo, Jakob and

Busch,³ Wigg,⁵¹ Masciottra,³⁵ and Bonarino-Udaondo⁴ Another case of Hart Hansen's,²⁰ was discarded for lack of pathologic proof

The chief symptomatology of all malignant tumors of the duodenum is that of duodenal obstruction, which varies more with the degree of obstruction than with the location of the growth in the duodenum (Eger¹⁶), except that peripapillary carcinoma produces jaundice much earlier than those of



FIG 4—Roentgenogram of the stomach and duodenum. Arrow points to the Y shaped irregularity in distal duodenum, which corresponds to the crater of the actual lesion

the other two segments. In the suprapapillary group, the onset was acute in about half the cases, the chief symptoms in order of frequency being vomiting, epigastric pain, weakness, weight-loss, jaundice and dyspepsia. Those with gradual onset complained of pain, dyspepsia, weight-loss, vomiting, and jaundice in that order. About one-fourth of the cases had a palpable mass in the region of the tumor. The usual roentgenographic picture was that of an ulcerating or obstructing lesion in the duodenum, though in some cases it was negative. The correct preoperative diagnosis was made only twice, and then from the roentgenograms. Roentgenologic studies are chiefly valuable in ruling out lesions of stomach, colon and gallbladder.

The usual pathologic picture is that of cylindrical cell carcinoma, though 121 cases of squamous metaplasia have been reported,³² and a few of malignant adenoma.²¹ Hoffman and Pack²¹ found that suprapapillary growths were most often of a hard, fibrous or colloid type, rather than scirrhous or polypoid. All three types usually obstruct the lumen and eventually neighboring structures. There is no conclusive evidence that suprapapillary cancer develops on the basis of simple ulcer. The incidence of metastasis is low, due probably to the rapid development of the disease and the early interference with vital functions. Hoffman and Pack²¹ report metastasis in 33 per cent of 18 cases, and quote Outerbridge's figure of 20 per cent in 125 cases, though Stewart and Lieber⁴⁵ found metastases in 75 per cent of their suprapapillary cases.

Results of treatment are very discouraging. Of course, there is no medical treatment for any duodenal carcinoma beyond palliation and supportive measures. Of 27 cases treated surgically to date, 20 had palliative or purely explorative procedures, with an operative mortality of 13 (65 per cent), while two were reported merely as operative recoveries, four died within the first year, and one at 3½ years after operation. In seven cases in which resections were attempted, three failed to survive operation (42.8 per cent), two are reported merely as operative survivals, one was alive for 3 months and another (Wig's⁵¹ case) for 7½ months after operation. The operation of choice is resection of the whole duodenal segment, with gastro-enterostomy if the bile and pancreatic ducts are not compromised. If they are, the procedure recommended below for peripapillary tumors is indicated. Palliative procedures are dictated by the pathology, gastro-enterostomy, with or without pyloric exclusion, for relief of alimentary obstruction, cholecystostomy or some type of gallbladder anastomosis for obstructive jaundice.

CARCINOMA OF THE PERIPAPILLARY PORTION

Of all duodenal carcinomata, this group is the most common (65 per cent) and, therefore, the most important. It is impossible to be certain of statistical data in this group because of many contradictions and the confusion of diagnosis in the literature. We have attempted to trace some of these discrepancies to their source and humbly offer the following conclusions, none too sure of their accuracy, since some original sources were not available. Though they themselves were found guilty of several misquotations, the study made by Lieber, Stewart and Lund,³¹ in 1939, was found to be the most critical, and we accept their figures as the most accurate available, with some corrections offered.

These authors carefully analyzed 399 cases reported up to 1939, but discarded 194, almost half, for lack of pathologic proof or insufficient data. To 205 acceptable cases, they added 17 new ones, making a series of 222 proven cases to 1939. We have analyzed 45 additional cases to date, of which 29 are acceptable as proven, bringing the current total up to 251.

The new cases are Fourteen reported by Cooper,¹² six by Hart Hansen,²⁰ three by Allen,¹ and one each by Cace,⁹ Duckworth,¹⁵ Gasbarrini,¹⁸ Hoshino and Abe,²² Orr,⁴² and Cabot,⁷ Case No 24162 Five cases reported from the roentgenographic standpoint only (four by Weintraub and Tuggle,⁴⁷ and one by Doub and Jones¹⁴), were excluded because of insufficient data Eleven cases, reported surgically, by Whipple,⁴⁹ in his excellent article on the surgery of this condition and of carcinoma of the head of the pancreas, have also been excluded from our statistics since no differentiation was made between the duodenal or pancreatic origin of the tumors

The relatively early development of obstructive jaundice (acute in 80 per cent) is the cardinal symptom of peripapillary carcinoma and was present in 99 per cent of the recorded cases The jaundice was accompanied by fever in 33 per cent of the cases The principal accompanying symptoms were pain (60 per cent), loss of weight and strength, anorexia, vomiting, constipation and diarrhea, in that order Very few patients presented any palpable mass, while 78 per cent had enlarged livers and half the cases had palpable gallbladders The correct preoperative diagnosis was made in 20 per cent of the cases, and was suspected, roentgenographically, in about 25 per cent Weintraub and Tuggle⁴⁷ reported a case in which the roentgenologic diagnosis was made by the discovery of air in the biliary tree, due to duodenobiliary fistula

The close proximity in this region of several complex and anatomically variable structures, and the early spread of cancer in the area to adjacent tissues, makes it very difficult to determine the exact site of origin of most peripapillary cancers and to exclude tumors arising in the bile ducts and pancreas From the standpoint of surgical therapy, such refinements are mainly academic, as the whole area, including the terminal bile and pancreatic ducts and the head of the pancreas may be considered as one unit, but for purposes of nosology an attempt at differentiation is necessary Lieber, Stewart and Lund³¹ classified 229 cases as follows

1. Primary carcinoma of the ampulla of Vater	3
2. Primary carcinoma of the terminal duct of Wirsung	1
3. Primary carcinoma of the terminal common bile duct	7
4. Primary carcinoma of the intestinal mucous membrane covering the papilla of Vater	3
5. Carcinoma involving all the epithelial structures comprising the papilla of Vater under Groups 1 2 3 and 4	182
6. Carcinoma involving all the epithelial structures comprising the papilla of Vater exclusive of the intestinal mucous membrane	33

Thus, 79 per cent of their cases fell into the large, indeterminate Group 5, despite very careful microscopic studies in many instances Hoffman and Pack²¹ believe that "carcinoma of the ampulla of Vater is not a true duodenal carcinoma, since it arises from the epithelium lining the terminal portion of the common bile duct The growth usually exhibits the histologic characteristics of the epithelium of the bile duct and may even develop true epidermoid carcinoma," of which they present an example Carcinomata of this region are frequently of the soft, bulky, polypoid variety, with an early

tendency to ulceration and bleeding,²¹ which accounts for the fact that about 20 per cent exhibit blood in the stool³¹—a guide to early diagnosis

From the viewpoint of etiology, Cohen and Colp¹¹ pointed out that the papilla and ampulla are exposed to the chronic irritation of an alkaline current from the ducts as well as the acid wash of the gastric contents. However, the higher incidence of carcinoma in this region may be due to the fact that the presence in this area of the duct epithelia, which are susceptible to carcinogenesis, outweighs the factor of relative immunity exhibited by the duodenal mucosa itself, for we have seen that it is usually impossible to tell the specific site of origin of most of the tumors

— In evaluating reported surgical results, one is confronted by contradictions in the reports of various authors, based on the loose interpretation of diagnostic criteria for one thing, and also on sheer misquotation in several instances. In 1927, Cohn and Colp¹¹ reviewed 59 cases treated by radical surgery, reporting an operative mortality of 44 per cent among 53 cases of transduodenal resection. In 1928, Busch⁶ reported nine survivals of one year or more, based mainly on Fulde's¹⁷ paper of 1927. Muller and Rade-maker,³⁸ in 1931, quoting Busch,⁶ reported eight survivals of four years or more, and are, in turn, quoted by Cooper.¹² In 1935, Hunt and Budd²⁴ collected 18 additional cases, which added to those of Cohn and Colp, comprised a series of 76 cases subjected to radical surgery with a mortality of 38.1 per cent. Allen,¹ in 1938, reviewed 97 reports of radical surgery (from the above papers) and found a 25.7 per cent survival of one year or more. Basing our present figures mainly on Lieber, Stewart and Lund's³¹ critical analysis of the original reports up to 1939, on our own review of the cases reported since then (analyzed by the same criteria), and on reference to original sources where discrepancies appeared among many of the above reports, we have concluded that to date, a total of 136 adequately proven cases of peripapillary carcinoma have been subjected to surgery of any type. In 122 cases, some operative result is known. Of these, 64 had purely palliative procedures for the relief of obstructive jaundice, with an operative mortality of 73.5 per cent, while in 58, radical resection of the primary tumor has been attempted alone or in combination with other procedures, with an operative mortality of 29.3 per cent. Of the latter group, the eight cases below, all of whom had transduodenal

Reported By	Year	Survival Period (Living and Well)	Final Authority for Survival Figure
1 Korte Case 32	1909	22 years	Busch [6] 1928
2 Olean	1919	4 years*	Olean [41] 1919
3 Lewis (Kelly's case)	1921	9 years*	Lewis [29], 1921
4 Kleinschmidt Case 2	1922	6 years	Lieber, Stewart and Lund [31], 1939
5 Tenani	1922	3 years*	Tenani [46] 1922
6 Fulde	1927	2 years	Fulde [17] 1927
7 Clär	1927	13 years	Nemenyi quoted by Lieber, Stewart and Lund [31] 1939
8 Lauwers Case 1	1933	3 years 10 mos	Lieber, Stewart and Lund [31] 1939

* Incorrectly cited by Lieber, Stewart and Lund³¹ as Olean 1 month, Lewis, 4 months, Tenani 5 months

resection, with or without other procedures, are known to have been living and well for two years or more after operation (13.8 per cent two-year cures), while four of these were alive and well five years or more (6.8 per cent five-year cures)

Also worthy of mention are Muller and Rademaker's³⁸ case, who died four years and eight months after operation, of metastases, and that of Judd, quoted by Cooper,¹² who was alive 2½ years after operation, but known to have a recurrence, both patients having also had transduodenal resections. Cabot's case, originally reported by Potter⁴⁴ as an eight-year cure, was excluded because it was a carcinoma of the common bile duct proximal to the duodenal segment, while three other cases, also reported by Muller and Rademaker³⁸ and Cooper¹² as five-year cures, were excluded because of insufficient data, namely, the cases of Oehler,⁴⁰ Van Remyse and Van Ardenne †

In the surgical approach to peripapillary carcinoma, the problem of re-establishing biliary and pancreatic continuity, especially the latter, has been most formidable. However, in 1935, Whipple, Parsons and Mullins⁵⁰ demonstrated that the reestablishment of pancreatic flow is not essential to life, thus increasing the prospect for a higher percentage of radical cures. The two-stage procedure which they evolved, as revised in 1938 by Whipple,⁴⁹ consists of a first stage, in which the common bile duct is ligated, the jejunum is sectioned and a cholecystojejunostomy and entero-anastomosis are performed according to the Y-principle of Roux. At the second stage, gastroenterostomy is performed, and is followed by a block resection, including the descending portion of the duodenum together with the distal portion of the common duct, and a V-shaped section of the head of the pancreas. The open duodenal ends are closed and the pancreatic ducts are ligated tightly. In 1941, Orr⁴² reviewed 15 cases of ampullary and pancreatic carcinoma treated by some variation of Whipple's principle, including one case of his own, and found a 33 per cent mortality, and 26.6 per cent survival (four cases alive 3 months, 4 months and 6½ months, and one an unknown period, post-operatively, respectively). In the exceptional case of very small tumors, simple excision may be radical enough to get wide of the growth, in others, the two-stage procedure of Whipple appears to be the operation of choice for the future. In very good risks, with adequate preoperative preparation, the two-stage operation is now undertaken in one sitting (Ziegler⁵²). Orr⁴²

† Oehler⁴⁰ originally reported his case in 1910 as alive and well three months after operation. Melchior,³⁶ in 1917, cited the same case as "alive one year, 11 months post-operative, slightly jaundiced, recurrence?" by personal communication of Kausch." This reference was misquoted by Fulde,¹⁷ in 1927, as a six-year cure, the error being perpetuated through Busch⁶ (1928) to Muller and Rademaker³⁸ (1931), and Cooper¹² (1937). The "cures" of Van Remyse (six years) and Van Ardenne (five years) were credited to a report by Klinkert,²⁶ in 1929, but reference to this source reveals no evidence whatever to consider these cases. They received only the briefest one-sentence mention by a discussor of Klinkert's paper, which reported an entirely different case.

suggests the use of lipocaic (pancreatic hormone) in combination with the above procedure.

CARCINOMA OF THE INFRAPAPILLARY PORTION

This group, in which our own case falls, is the smallest of the three (15 per cent) Stewart, Lieber and Lund³⁰ analyzed 62 reported cases, accepted 36 as authentic, and added two of their own, making a total of 38 proven cases up to 1937. We have analyzed 19 additional cases, all proven, which, with our case, bring the total known to date to 58. The new cases are: Six reported by Hoffman and Pack,²¹ three by Hart Hansen,²⁰ two by Bergendahl,² and one each by Howes,²³ Hadfield-Jones,¹⁹ Allen,¹ Claiborn and Dobbs,¹⁰ Brunschwig and Childs,⁵ Pollack,⁴³ MacIndoe,³³ and Cabot.⁸ Case No 27092.

The principal symptoms were pain, vomiting and cachexia, regardless of type of onset, while anorexia, constipation, diarrhea and jaundice were found less commonly. Only 16.6 per cent had a palpable mass in the region of the tumor.³⁰ The preoperative diagnosis was rarely made. Lieber, Stewart and Lund³⁰ found in a series of 15 cases studied roentgenographically that an obstructing lesion of the duodenum was present in 40 per cent, in 33 per cent the lesion was incorrectly diagnosed as at or near the pylorus, while in 27 per cent no lesion was demonstrable.

The usual pathologic picture was that of a broad, flat, ulcerating mass, as in our case. The average size was 3-5 cm in diameter in the majority of cases.

TABLE I
DISTRIBUTION OF CASES AND RESULTS OF SURGICAL THERAPY OF
PRIMARY CARCINOMA OF THE DUODENUM

Primary Carcinoma of Duodenum	Suprapapillary	Peripapillary	Infrapapillary	Total
Total No. of reported cases	125	461	84	670
Distribution in duodenum	18 6%	68 8%	12 5%	
Total No. accepted as proved	77	251	58	386
Distribution in duodenum	19 9%	65 0%	15 0%	
Total subjected to surgery	27	136	33	196
Palliative surgery	20	64	22	106
Operability	25 9%	25 4%	37 9%	27 2%
Op. mortality	65 0%	73 5%	90 0%	75 5%
Radical surgery	7	58	11	76
True operability	9 0%	23 1%	18 9%	19 6%
Op. mortality	42 8%	29 3%	33 3%	31 0%
No. alive and well at 2 years	0	8	0	8
Per cent 2-yr. cures	0	13 8%	0	10 5%
No. alive and well at 5 years	0	4	0	4
Per cent 5-yr. cures	0	6 8%	0	5 2%

To date, there are 33 reported cases in which surgical therapy has been applied. Of these, 22 had purely palliative or exploratory operations, in two of which the results are not recorded. Of the 20 known results, 18 were immediate operative mortalities (90 per cent), while all were dead in three months. Eleven radical resections have been attempted, in two of which no results are recorded. Of the nine known results, three were operative mortalities (33 per cent), while six were successful. Of these, three patients

were alive at three months, and three at 15, 16 and 20 months after operation (the cases of Brunschwig and Childs,⁵ Hadfield-Jones¹⁹ and Bergendahl,² respectively)

Since the bile and pancreatic ducts are not involved, the operation of choice for infrapapillary tumors is resection of the affected segment and reestablishment of alimentary continuity by duodenojejunostomy, end-to-end, end-to-side, or side-to-side. Hadfield-Jones¹⁹ brought the jejunum to the right, under the superior mesenteric artery, until it lay in position for anastomosis to the proximal duodenal segment without tension. Lahey's²⁸ plan of antecolic duodenojejunostomy, recommended for high jejunal lesions, may also be applied to infrapapillary duodenal lesions.

SUMMARY AND CONCLUSIONS

A proven case of primary carcinoma of the infrapapillary portion of the duodenum is presented, and discussed from the point of view of clinical roentgenographic, operative and autopsy findings.

The literature on all types of primary duodenal carcinoma is reviewed, covering a total of 386 proven cases to date, of which 19.9 per cent were suprapapillary, 65 per cent papillary, and 15 per cent were infrapapillary.

Each subgroup is briefly considered from the standpoint of incidence, principal symptomatology, roentgenographic findings, pathologic picture and recorded surgical results. The latter are summarized in Table I.

Earlier diagnosis depends on a better awareness in the mind of the clinician that the diagnosis of duodenal carcinoma is possible though rare (from 0.3 per cent to 0.03 of all autopsies). Roentgenologic examination is especially helpful if the lesion is looked for consciously.

While the results of radical surgery in duodenal carcinoma so far have been very discouraging (5.2 per cent five-year cures), with earlier diagnosis and with improved methods of pre- and postoperative care, such as exist today, the prospect for improved results in the future looks brighter, since a rational surgical technic is available for each group of cases, and since metastasis at the time of exploration is low.

BIBLIOGRAPHY

- ¹ Allen, C. I. Primary Cancer of the Duodenum. Report of 11 Cases. *Am J Surg*, 40, 89, 1938.
- ² Bergendahl, A. A Contribution to the Knowledge of Primary Duodenal Cancer. *Acta Radiologica*, 20, 417, 1939.
- ³ Bolo, P. O., Jakob, R., and Busch, W. E. Supravaterian Cancer of the Duodenum. Pyloroduodenectomy with Surgical Healing. *Bol y trab de la Soc de cir de Buenos Aires*, 22, 722, 1938.
- ⁴ Bonarino-Udaondo, C. Primary Cancer of the Duodenum. *Prese Med Argent*, 28, 1018, 1941.
- ⁵ Brunschwig, A., and Childs, A. Resection of Carcinoma (Carcinoid?) of the Infrapapillary Portion of the Duodenum Involving the Ampulla of Vater. Reimplantation of the Common and Pancreatic Ducts. *Am J Surg*, 45, 320, 1939.
- ⁶ Busch, E. Et Tilfaelde af operativt behandlet carcinoma papilla Vateri. *Hospitalstid*, 71, 1415, 1928.

- 7 Cabot, Case No 24162 Carcinoma of the Duodenum *N Eng J Med*, 218, 687, 1938
- 8 Cabot, Case No 27092 Primary Carcinoma of the Third Portion of the Duodenum *N Eng J Med*, 224, 386, 1941
- 9 Cace, M Primary Tumors of the Duodenum and Jejunum *Lymphogranuloma of the Duodenum* *Radiol Med*, 25, 365, 1938
- 10 Claiborn, L N, and Dobbs, W G H Carcinoma of the Third Segment of the Duodenum *Surgery*, 4, 97, 1938
- 11 Cohn, I, and Colp, R Cancer of the Periapillary Region of the Duodenum *S G and O*, 45, 332, 1927
- 12 Cooper, W A Carcinoma of the Ampulla of Vater *ANNALS OF SURGERY*, 106, 1009, 1937
- 13 de Candia, S Primary Cancer of the Duodenum A Review *Riforma Med*, 55, 809, 1939
- 14 Doub, H P, and Jones, H C The Roentgenologic Diagnosis of Tumors of the Small Bowel *Am J Dig Dis*, 8, 149, 1941
- 15 Duckworth, W D Primary Cancer of the Duodenum *Am J Roentgen*, 40, 377, 1938
- 16 Eger, S A Primary Malignant Disease of the Duodenum *Arch Surg*, 27, 1087, 1933
- 17 Fulde, E Die bekanntgewordenen Ergebnisse der Radikaloperationen der Gallengangskrebse *Zentralb f Chir*, 54, 1481, 1927
- 18 Gasbarrini, A Primary Adenocarcinoma of the Duodenum *Il Policlinico*, 56, 1787, 1939
- 19 Hadfield-Jones, P M Intrinsic Carcinoma of the Duodenum Report of Successful Removal *Lancet*, 2, 1168, 1938
- 20 Hart Hansen, E Cancer of the Duodenum—Primary and Secondary *Acta Chir Scandinav*, 80, 295, 1938
- 21 Hoffman, W J, and Pack, G T Cancer of the Duodenum, A Clinical and Roentgenographic Study of 18 Cases *Arch Surg*, 35, 11, 1937
- 22 Hoshino, M, and Abe, M A Case of Primary Duodenal Cancer *Bull Naval Med Assn of Japan*, 29, 51 (Abstract Section), 1940
- 23 Howes, W E The Duodenum, Roentgenographically Considered Including One Case of Primary Carcinoma *N Y S J Med*, 37, 1997, 1937
- 24 Hunt, V C, and Budd, J W Transduodenal Resection of the Ampulla of Vater *S G and O*, 61, 651, 1935
- 25 Jerrell, P M Huntington's Chorea, Adenocarcinoma of Duodenum and Chronic Encephalitis *Med Bull Vet Adm*, 13, 269, 1937
- 26 Klinkert, H Over Carcinoma Duodeni ad Papillam Vateri *Nederl tijdschr v geneesk*, 73, 4443, 1929
- 27 Lahey, F H Surgery of the Duodenum *N Eng J Med*, 222, 444, 1940
- 28 Lahey, F H A New Plan of Antecolic Duodenojejunal Anastomosis *S G and O*, 70, 689, 1940
- 29 Lewis, R M Cancer of the Ampulla of Vater *S G and O*, 32, 543, 1921
- 30 Lieber, M M, Stewart, H L, and Lund, H Carcinoma of the Intrapapillary Portion of the Duodenum *Arch Surg*, 35, 268, 1937
- 31 Lieber, M M, Stewart, H L, and Lund, H Carcinoma of the Peripapillary Portion of the Duodenum *ANNALS OF SURGERY*, 109, 219 and 383, 1939
- 32 Lieber, M M, Stewart, H L, and Morgan, D R Adenosquamous Carcinoma of the Periapillary Portion of the Duodenum *Arch Surg*, 40, 988, 1940
- 33 MacIndoe, P H A Case of Carcinoma of the Infra-ampullary Part of the Duodenum *M J Australia*, 1, 148, 1940
- 34 Mateer, J G, and Hartman, F W Primary Carcinoma of the Duodenum Clinical and Pathologic Aspects, with Differential Diagnosis *J A M A*, 99, 1853, 1932

- ³⁵ Masciottra, R L Primary Carcinoma of the Duodenal Bulb Rev Assoc Med Argent, 53, 820, 1939
- ³⁶ Melchior, E Die chirurgie des Duodenum Neue Deutsche Chir, 25, 328-358, 1917
- ³⁷ Meyer, J, and Rosenberg, D H Primary Carcinoma of the Duodenum Arch Int Med, 47, 917, 1931
- ³⁸ Muller, G P, and Rademaker, L End Results in Radical Operations for Carcinoma of the Periapillary Region of the Duodenum ANNALS OF SURGERY, 93, 755, 1931
- ³⁹ Nicolini, R C Primary Cancer of the Duodenum Bol y trab de la Soc de cir de Buenos Aires, 22, 666, 1938
- ⁴⁰ Oehler, J Beitrag zur Kasuistik und Diagnose des Primaren Carcinoms der Papilla Vateri Beitrage z Klin Chir, 69, 726, 1910
- ⁴¹ Oleani, E Per la Casuista del Carcinoma della Papilla del Vater Clin Chir, 26, 898, 1919
- ⁴² Orr, T G Resection of the Duodenum and Head of the Pancreas for Carcinoma of the Ampulla S G and O, 73, 240, 1941
- ⁴³ Pollack, S Primary Carcinoma of the Third Portion of the Duodenum Radiology, 31, 362, 1938
- ⁴⁴ Potter, E B Successful Resection of the Common Biliary Duct for Carcinoma of the Ampulla of Vater ANNALS OF SURGERY, 98, 369, 1933
- ⁴⁵ Stewart, H L, and Lieber, M M Carcinoma of the Suprapapillary Portion of the Duodenum Arch Surg, 35, 99, 1937
- ⁴⁶ Tenani, O Contributo alla chirurgica della papilla de Vater Policlinico (sez chir), 29, 291, 1922
- ⁴⁷ Weintraub, S, and Tuggle, A Neoplasms Involving the Duodenum Radiology, 28, 362, 1937
- ⁴⁸ Woods, J O Primary Carcinoma of the Duodenum Penn Med Jour, 41, 27, 1937
- ⁴⁹ Whipple, A O Surgical Treatment for Carcinoma of the Ampullary Region and Head of the Pancreas, Am J Surg, 40, 266, 1938
- ⁵⁰ Whipple, A O, Parsons, W B, and Mullins, C R Treatment of Carcinoma of the Ampulla of Vater ANNALS OF SURGERY, 102, 763, 1935
- ⁵¹ Wing, N A Case of Primary Cancer of the Duodenal Bulb Nord Med, 2, 1767, 1939
- ⁵² Ziegler, H R Excision of the Head of the Pancreas for Carcinoma Studies of its Blood Supply S G and O, 74, No 2, 137, 1942

SOLITARY NONPARASITIC CYST OF THE LIVER

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SOLITARY NONPARASITIC CYST OF THE LIVER occurs sufficiently rarely to warrant the report of every such cyst encountered. In 1937, Davis¹¹ extensive study of nonparasitic cysts of the liver revealed 187 reported cases of a solitary cyst, to which he added one. Eight years previously, Stoesser and Wangenstein's³⁸ review placed the number of reported cases at 104. Och-sner²⁷ reported a case in 1937. Jennings¹⁵ added a case in 1939, and during the same year Attix² reported another. In 1940, Montgomery²³ added two cases.

Although reported cases include all ages from fetal life to extreme old age, the disease most commonly presents itself between the ages of 40 to 60. As stated by Montgomery²³ (including his two reported cases) in 1940, there have been only 27 cases under the age of 13. No doubt, as is true in all diseases, there have been others that have not found their way into the literature.

I should like to report a case that presented a solitary nonparasitic cyst of the liver which recently came under my care.

Case Report—M S, male, age nine months, was readmitted to the Charlotte Memorial Hospital, September 7, 1941, with an enlarged abdomen since the age of six weeks. The family history was essentially normal. The child was born at full term by normal delivery. The birth weight was eight and one-half pounds (3855.60 Gms). The child had never eaten well. He nursed only fairly well, and there was frequent regurgitation. He had had no acute sickness other than a "spell of flu" at age two months. The child gained fairly normally up until age six-seven months, since which time he had gained rather poorly. After birth and up until he was four months old, he would never have regular bowel movements, but his diapers were almost constantly spotted. This condition was checked by therapy, but since then there had been some trouble with constipation.

The mother noted that the child's abdomen was too large at age six weeks when "navel bands" were being used. She did not pay a great deal of attention to this, but she became alarmed when she noted a hard lump in the right upper quadrant when he was six months old. Dr. E. K. McLean of the Pediatric Department of the Charlotte Memorial Hospital was consulted. He informed the parents that a tumor was present, and studies were ordered. Dr. Robert W. McKay of the Urological Department studied the kidney status, and it was his opinion that the tumor did not originate from the kidney. Dr. Allan Tuggle of the Radiology Department reported "A flat film of the abdomen reveals a huge mass in the right abdomen. On some of the films a normal-sized kidney shadow is seen through this mass. The spine is not unusual."

"A barium enema shows the colon to fill completely with no defects or spasms. The mass depresses the hepatic flexure and the midtransverse colon (Fig. 1)."

"A pyelogram on the following day after injection of five cc of diodrast shows excretion from each side. A 10, 20, 30, 50, and 70 minute film shows poor function. The mass previously seen on the flat film is excluded as being kidney."

"From the radiographs I doubt that this is a renal neoplasm but would suggest that it is liver."

It was decided to determine whether roentgenotherapy would diminish the size of the mass. Through the anterior right upper quadrant 400 R and 350 R through the lateral right upper quadrant failed to decrease the size of the mass.

Physical Examination—Temperature to be 98°F, pulse 84, respiration 18. The patient was a well-developed and well-nourished white male of nine months, with a

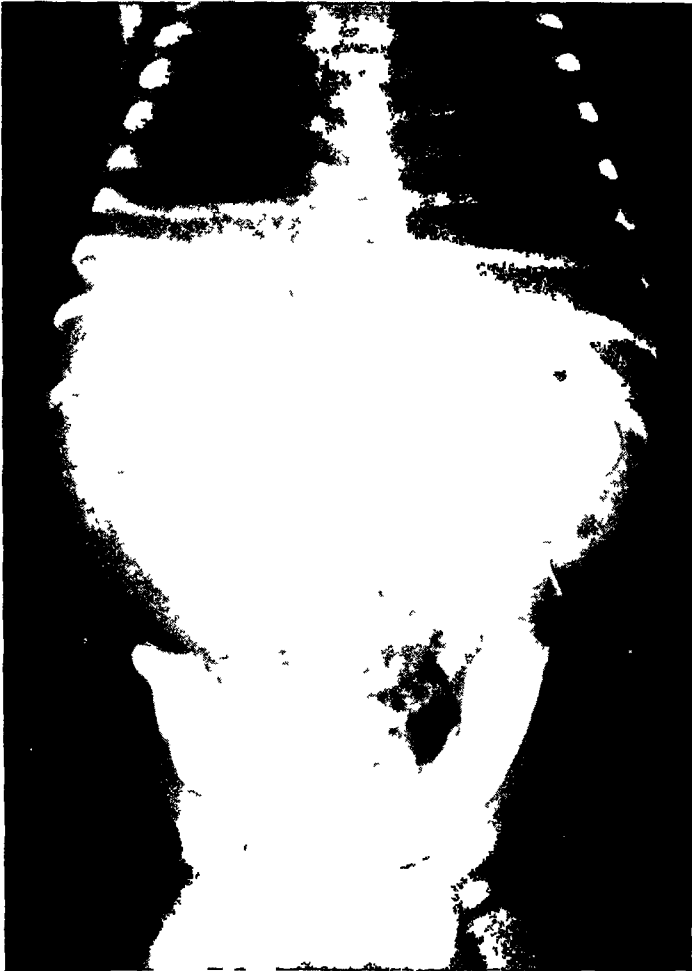


FIG 1—Preoperative roentgenogram after barium enema, showing the marked displacement of the colon medially and inferiorly by the large mass occupying the right upper abdomen. As pointed out by Hofmann, this is a most important sign in the diagnosis of liver cysts.

greatly enlarged abdomen. Head: Normal bony contour. Eyes: Reacted actively to light. Ears: Essentially normal. Nose and Throat: Essentially normal. Heart and lungs: Negative. Abdomen: There was a large, firm, apparently nontender mass about the size of a grapefruit which filled almost the entire right side of the abdomen, especially the right upper quadrant. The mass was fairly movable and seemed to be smooth-walled. There was a visible prominence of the right upper quadrant with a definite flaring of the right costal arch. There were no herniae, scars, or tenderness of the abdomen. Spleen was not palpable. There were no enlarged lymph nodes. External genitalia: normal male development. Extremities: were normal.

Laboratory Data—Hb 60 per cent, WBC 11,900, RBC 3,900,000, Differential essentially normal, Wassermann and Kahn tests negative. Urinalysis: essentially normal.

Impression and Preoperative Diagnosis—Most likely either a mesenteric or omental cyst.

Operation—September 7, 1941 (H S M, Jr) The patient was given a subcutaneous infusion of 300 cc of saline. Under drop-ether anesthesia, the abdomen was opened through a long right midrectus muscle-splitting incision. A large smooth-walled mass, which completely filled the upper right side of the abdomen and a great portion of the right lower abdomen, presented itself. It was immediately apparent that this mass was densely incorporated into the right lobe of the liver. It measured about 12 cm in diameter, and although firm, it was suggestively cystic. The mass, along with a portion of the liver, was delivered through the incision, which was necessary because it was

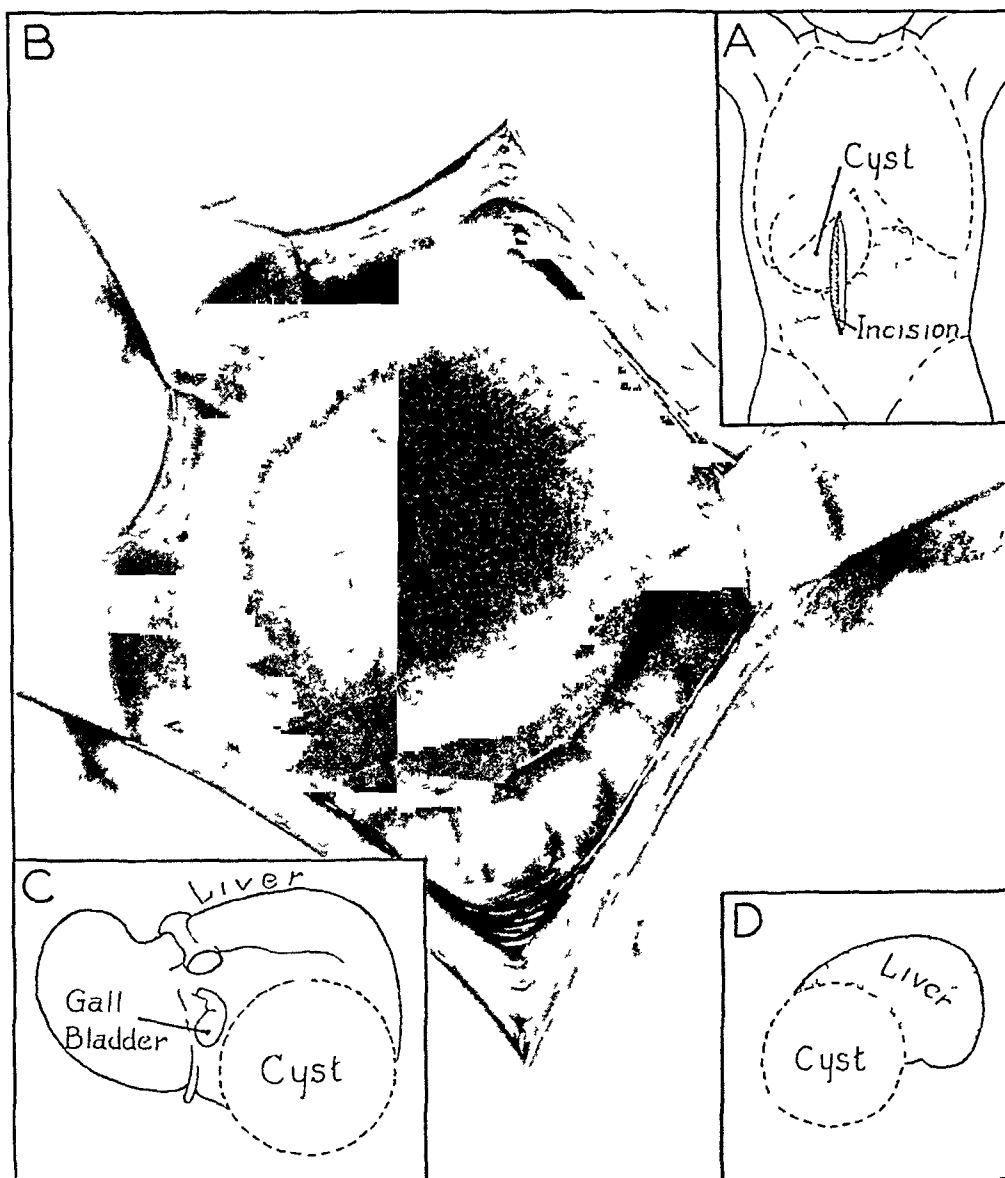


FIG 2—Appearance and anatomic relationship of the mass upon operative exposure

not readily accessible for aspiration. The delivery of the mass and partial delivery of the liver occasioned some shock. The stomach, duodenum, large bowel, and small bowel were all displaced to the left and inferiorly (Fig 2). An aspirating needle was inserted a distance of fully 2.5-3 cm, when clear straw-colored fluid was encountered and aspirated. After a portion of the fluid had been aspirated, the mass was returned into the abdominal cavity. The gallbladder lay just to the left of the involved portion of the right lobe of the liver. The cyst had taken up fully one-half to two-thirds of the right lobe of the liver. Normal liver tissue could be recognized on the anterosuperior portion

of the cyst, but it was impossible to find a sharp line of demarcation between the grossly normal liver tissue and the wall of the cyst. Abdominal palpation revealed no apparent renal enlargement or pancreatic enlargement that would be suggestive of polycystic disease. The cystic mass was then incised at the point of aspiration. Fluid was removed by suction. Its quantity was not accurately measured although a specimen was saved for study. The interior of the cyst was smooth-walled, and there were several membranous folds partially traversing the cavity. At its most inferior portion the cyst wall was approximately two cm in thickness. This apparently was the thinnest portion of the wall. An adequate portion of the wall was removed for pathologic study. The cavity of the cyst extended far up into the central portion of the right lobe of the liver. One gained the impression that the cyst most probably had its origin deep within the right lobe of the liver, and that the wall of the cyst was composed of atrophic liver tissue. The intrinsic pressure of the cyst was apparently low. It was apparent that the child would never survive any attempt at complete extirpation of the cyst, hence, marsupialization of the cyst wall to the peritoneum was elected. A portion of the incised cyst was closed with interrupted No 2 chromic catgut. The peritoneum and posterior rectus sheath were approximated with continuous No 1 plain catgut. Due to the extreme thickness of the wall of the cyst it was impossible to bring the cyst wall up to the skin margin. The peritoneum and posterior rectus sheath were sutured to the cyst wall about the opening of election in the wall of the cyst. The anterior rectus sheath was approximated with interrupted sutures of fine black silk above and below the opening. Through a large Penrose drain a number of gauze strips that had been saturated with Zenker's solution (solution of bichloride of mercury 5 per cent, and potassium dichromate 2.5 per cent) were inserted into the cyst cavity. The patient left the operating room in fair condition. *Postoperative Diagnosis*: Solitary nonparasitic cyst of the liver.

Pathologic Examination—Microscopic: Dr Paul Kimmelstiel "Histologic sections through the wall of the cyst show that the latter is mainly composed of rather a cellular connective tissue in which are found numerous bizarre-shaped ducts lined by a single layer of low cuboidal epithelial cells. The lumen of many of the ducts is open, but some of them are not patent. The ducts and capillaries are irregularly arranged and surrounded by concentric layers of laminated connective tissue. In some areas a collection of large polygonal epithelial cells is seen, the cells have clear borders and the cytoplasm is vacuolized. The nucleus is located in the center. The cells are not in distinct arrangement, they do not form glands, but they occur in columns and nests, separated from each other by capillaries which can be readily identified as they are lined by endothelial cells. These groups of cells are suggestive of vacuolized liver cells which do not bear cilia. The inner lining of the cyst is in continuity with a number of bay-like extensions which in turn are continuous with the above described ducts in the wall of the cyst.

"Chemical examination of fluid from cyst: Specific gravity 1.010, N P N 13 mg per cent, cholesterol very faint trace, bile negative, urobilinogen negative, hemoglobin negative, total protein 1.5 Gm per cent. *Pathologic Diagnosis*—Congenital cyst of liver derived from bile ducts" 11

Postoperative Progress—Following operation there was a febrile reaction, the rectal temperature rising to 104.4°F on the evening of the day of operation, but this gradually subsided. The gauze pack was removed from the liver cyst on the second postoperative day, and a soft rubber catheter was inserted. Drainage was only moderate. At no time was there any gross or clinical evidence of bile. On the ninth postoperative day, the temperature suddenly rose to 104°F, but rapidly subsided with sulfathiazole therapy. The cyst was daily irrigated with Dakin's solution. Frequent measurements demonstrated gradual diminution in the size of the cyst. One month after operation a roentgenogram taken following injection of lipiodol through the catheter showed a cavity of about two cm in size (Fig 4). The liver shadow was still large. The

cyst was frequently flooded with Zenker's solution which seemed to produce little or no generalized reaction

Subsequent Course—The child was discharged from the hospital, October 15, 1941, five weeks after operation, and was seen at weekly intervals, the catheter being irrigated with Zenker's solution without any untoward reaction at each visit. The cavity gradually reduced to one cm in size. The catheter was gradually removed and the tract was packed with iodoform gauze. This gauze was gradually displaced by granulation tissue. Abdominal palpation, March 30, 1942, revealed an oblong, nontender, firm mass that extended from the area of marsupialization to the liver. This was taken to be the obliterated cyst of the liver. There was a small granulating area at the region of the



FIG. 3—Top Cyst wall under low power showing fibrous tissue with bile ducts. On the left of the midline is nest of liver cells.
Lower right Outpouching of cyst, showing high cylindrical cells lining the inner wall.
Lower left Cyst wall under high power showing small bile ducts partially with and partially without demonstrable lumen.



Fig 5.—Photograph taken, March 24, 1942. The upper abdomen seems rather full. The mass can be palpated, but is considerably reduced in size. The sinus tract is closed, and there is no drainage.



Fig 4.—Postoperative roentgenogram, October 8, 1941, following injection of lipiodol through a catheter placed at the point of marsupialization.

marsupialization that is rapidly healing under treatment with silver nitrate. The sinus tract was obliterated. The child is growing and developing normally, and appears to be in the best of health (Fig. 5).

Nonparasitic cysts of the liver may be single or multiple. Multiple cysts may be confined to the liver alone, but more commonly they are associated with cysts of the kidneys, pancreas, spleen, lungs, and brain. Multiple cysts are more common in children than in adults, and may be associated with other congenital malformations as harelip, cleft palate, and spina bifida. Solitary nonparasitic cysts are more common in adults. Whether justifiable or not it is customary to differentiate sharply between solitary and multiple nonparasitic cysts of the liver. Boyd⁸ and Sonntag³⁶ are inclined to believe that cystic disease and solitary cysts of the liver are different manifestations of the same disease. Stoesser and Wangenstein³⁸ state as follows: "It is generally accepted that solitary cysts in nonarteriosclerotic kidneys are but another expression of polycystic disease, a corresponding similarity would appear to extend to the manifestation of the disease in the liver. In several cases reported on solitary cysts of the liver, there have been small cysts in the proximity of the large cyst." Whether the solitary cyst of the liver is a lonesome manifestation of polycystic disease or an entirely unrelated abnormal process is a debatable issue. Until more is known, and for the sake of clarity, let us refer to these two conditions as definitely separate entities. In the reports of some writers this differentiation has not been sharply adhered to.

Cysts seem to occur more often in females than in males, the ratio being 4:1. This is explained on the basis that developmental defects are well known to be more common in the female sex.

The earliest reported case of cystic disease of the liver was that of Bristowe in 1856. This was the postmortem finding in a 53-year-old shoemaker. To substantiate the congenital origin of these cysts and to illustrate the age variations, let us review some of the reports. In 1880, Witzel⁴⁴ reported a case of a large liver cyst in a newborn which complicated labor. In the same year Sanger and Klopp³² reported a very similar case. In 1892, Bagot³ reported a case with a liver cyst containing two and one-half gallons of fluid which, of course, interfered with delivery. The oldest patient with nonparasitic cyst of the liver was reported by Bland-Sutton⁶ in 1905. This was in a man, age 75.

PATHOLOGIC ANATOMY

Reference has already been made regarding solitary and multiple nonparasitic cysts of the liver. Solitary cysts are most commonly found at the antero-inferior portion of the right lobe of the liver. The quadrate lobe and the left lobe are sometimes involved, and in still fewer cases, the cyst occupied the central portion of the liver. In one case described by Montgomery,²³ and in a few cases described by Harrington,¹³ the round ligament was involved. The size of the cyst and the amount of liver destruction vary considerably. Some cysts are microscopic, and some may fill the abdomen. An

entire lobe of the liver may be destroyed by the cyst. The cyst may be wholly or partially intrahepatic, or it may be pedunculated. Little is known about the growth of these cysts, but apparently growth is so tardy that adjacent viscera quickly adapt themselves to its presence without symptoms as a rule. In contradistinction to *echinococcus* cysts, these cysts have a characteristic low internal tension.

The external surface of these cysts is usually smooth, glistening, and grayish-blue, often showing many dilated veins. The appearance may be not unlike that of a large smooth-walled cyst of the ovary. The internal surface is usually smooth, less regular, and is usually trabeculated. The thickness of the cyst wall is variable. There is usually no definite line of cleavage between the intrahepatic and partially intrahepatic cyst wall and the normal liver tissue.

The cystic contents vary from a clear, watery, sometimes yellowish-brown fluid, neutral or alkaline in reaction, with a specific gravity varying from 1.007 to 1.024 to a semisolid material resembling an organized clot, as in the case reported by Montgomery.²³ An analysis of the cystic fluid may show albumin, mucin, cholesterol, blood, hematoidin, hemosiderin, tyrosine, some granular and cellular debris, and rarely bile. Some writers claim that the older cysts contain no bile because it is being constantly absorbed. In explanation of the presence of bile in some cysts, Boyd⁸ ventured to say that if the cyst increases in size, large intrahepatic bile ducts rupture into the cyst, their walls being destroyed by pressure. This explanation would appear to find support in the fact that following drainage of the cyst, bile has been known to escape through the drainage tube when the contents of the cyst at operation failed to show bile pigments.

The microscopic appearance of the cyst wall, according to various authorities, consists of three layers of connective tissue, an inner layer rich in cellular element, a circularly arranged dense layer poor in cell nuclei and containing a few blood vessels with thickened intima, a loose outer layer with elastic fibers, muscle bundles rich in cells, many blood vessels and bile ducts. The cyst is lined with cubical, cylindrical, or flat cells, but the epithelium is much desquamated. The bile ducts found in the walls of the cysts are usually lined with the same kind of epithelium which lines the cyst.

The most generally accepted classification of nonparasitic cysts of the liver is that of Sonntag.³⁶ "(a) Blood and degenerated cysts, (b) dermoid cysts, (c) lymphatic cysts due to obstruction or to congenital dilatation of the lymphatics, (d) endothelial cysts, (e) cysts due to bile duct obstruction, and (f) proliferative cysts (cystadenoma)."

The possible mode of origin of these cysts has been discussed at length by Siegmund,³⁵ von Kahlden,⁴⁰ Neuwerk and Hufschmid,²⁶ Borrmann,⁷ Kaufman,¹⁷ Konjetzny,¹⁸ Sternberg,³⁷ Plenck,³¹ Burns,⁹ Jones,¹⁶ Bland-Sutton,⁶ Moschowitz,²⁴ McGlannon,²² and Henke.¹⁴

There is considerable discrepancy in regard to the histiogenesis depending on the individual interpretation of histologic findings. Consequently, no classification of nonparasitic cysts of the liver is yet presented which has

found general acceptance Heixheimer,¹⁴ in his description of cystadenoma of the liver (cysts), correctly emphasizes this point

DIAGNOSIS AND CLINICAL FEATURES

Solitary nonparasitic cysts of the liver apparently grow so slowly that in most instances, few if any symptoms are produced, advice usually being sought because of the presence of a painless abdominal swelling. Occasionally, however, there may be a sudden onset of acute symptoms. This is seen, for instance, when an acute hemorrhage occurs into the cyst, when suppuration supervenes, or when, in the pedunculated variety, the pedicle becomes twisted. A correct preoperative diagnosis is rarely made, the majority of the cases being diagnosed on exploratory celiotomy or at necropsy. There is only one case reported with a correct preoperative diagnosis. Kilvington, of Melbourne (where hydatid cysts are common), made this diagnosis on the basis of the low internal tension of the cyst.

This condition is usually symptomless unless complications occur or the cyst compresses some adjacent structure such as the extrahepatic bile ducts or the first portion of the duodenum. With compression, there may be acute hepatic pain, nausea, vomiting or jaundice. As most of these cysts arise from the antero-inferior surface of the right lobe of the liver, clinical examination will determine the site of the tumor while radiography may show that the tumor is part of the liver. One of the most important signs is that pointed out by Hofmann. With large cysts or tumors of the liver, the colon is pushed downward and to the left of the abdomen, while in the case of neoplasm or other enlargements of the kidney, the colon lies over the tumor. This point may be easily demonstrated by barium enema. In my opinion, this a very important diagnostic criterion.

In the case of all large pedunculated cysts of the liver, downward displacement is limited by anchorage to the liver, but a considerable degree of lateral movement is often obtained. Induced pneumoperitoneum followed by roentgenologic examination has proven of little help. Peritoneoscopy may be an aid in diagnosis. Liver function tests, as a rule, show little deviation from the normal. I do not intend to enter into a detailed discussion of the differential diagnoses at this time.

TREATMENT

The only treatment for solitary cysts of the liver demanding relief is surgical intervention. Complete extirpation of the cyst should be undertaken if conditions permit. Too frequently, this procedure cannot be wisely attempted without inviting disaster. Partial extirpation along with drainage and marsupialization, or just drainage along with marsupialization have produced satisfactory end-results in most cases. In some instances in which external drainage has been done, a sinus has remained for from a few months to years. In Evans' case a sinus persisted. Jones¹⁶ stated that in Theodoroff's

case a sinus remained for 37 months following drainage of a nonparasitic cyst. Porter's patient developed a chronic sinus and the patient died following an attempt to correct this condition surgically. Fatalities have been reported which were due to shock from the sudden release of intra-abdominal pressure. This can be avoided by the injection of epinephrine hydrochloride subcutaneously before the cyst is opened, and by slow removal of the fluid. The prognosis is good if the patient survives operation, but the operative mortality of nonparasitic cyst of the liver in reported cases varies between 10 and 30 per cent.

COMMENT—In my case I should like to stress the extreme thickness of the cyst wall, and the fact that a large portion of the cyst was intrahepatic. Although the fluid content of the cyst was aspirated by needle the cyst showed no tendency to collapse. The thickness and rigidity of the wall would not have permitted any radical removal of the cyst, nor would an adequate closure have been possible after such a procedure, furthermore, this patient would not have survived such a radical attempt at removal of the cyst. These considerations prompted the operative procedure adopted. A portion of the wall was excised for pathologic study, and the cyst wall was marsupialized to the peritoneum and the posterior rectus sheath. No collapse of the thick wall of the cyst was anticipated. The lining was frequently treated with Zenker's solution to facilitate the eventual obliteration of the cavity by granulation tissue. The end-result is quite satisfactory.

Our case, as well as the majority of similarly treated ones, may throw some light upon the nature of such nonparasitic cysts of the liver which are lined by epithelial cells. It is generally agreed that these cysts, and they represent the majority of cases, are derived from congenital malformations. The mode of growth, however, has not satisfactorily been explained.

With the exception of such few cases, in which histologic examination revealed evidence of the carcinomatous character of a papillary cystadenoma, the true blastomatous nature of liver cysts is still questionable.

They can readily be classified as hamartomata in the sense of Albrecht, as malformations based upon disproportion anlage of tissue elements.

The enlargement may be explained by gradual increase of fluid with proportionate increase in number of lining epithelial cells within physiologic limits. Adjacent smaller cysts may merge into the larger one. Pressure upon the surrounding liver tissue may result in atrophy. The latter, as commonly observed in cirrhosis or other scars of liver tissue, is associated with proliferation of bile ducts. Proliferating bile ducts, therefore, in the wall of liver cysts, as observed in our and other cases, does not necessarily indicate the true blastomatous nature of the cyst. Secondly, they may communicate with the main lumen but can readily be interpreted as the result rather than the origin of the cyst.

This interpretation in my opinion seems likely because our case as well as other similarly treated cases have shown an obliteration and complete cure following destruction of the inner epithelial lining. If the tortuous bile

ducts deep in the thick fibrous wall of the cyst would truly be blastomatous in nature, the majority of cysts would have shown recurrence

It is for this reason that I believe that epithelial-lined cysts, which fail to show active papillary growth, should be classified as hamatomata rather than cystadenomata in the sense of true blastomata

SUMMARY

A solitary nonparasitic cyst of the liver in a nine months old child is presented. Because of the impossibility of complete extirpation drainage and marsupialization was done. The end-result is very satisfactory, a complete cure being anticipated. Reasons are presented for a classification of this liver cyst as hamatoma rather than cystadenomatous blastoma.

Grateful acknowledgment is made of the help of Dr. Paul Kimmelstiel, of the Department of Pathology, Dr. Allan Tuggle, of the Radiology Department, Dr. Robert W. McKay, of the Urological Department, and Dr. E. K. McLean, of the Pediatric Department of the Charlotte Memorial Hospital, Charlotte, N. C.

REFERENCES

- ¹ Alexander, R. C. Solitary Nonparasitic Cysts of the Liver. *Edinburgh M. J.* 32: 61 (Feb.) 1925
- ² Atlix, F. F. Nonparasitic Cysts of the Liver. *Lancet*, 59, 38, February, 1939
- ³ Bagot, W. S. Dystocia Due to a Cyst in the Liver of a Fetus. *Dublin M. J. Sc.*, 93, 265, April, 1892
- ⁴ Bayer, C. Über eine durch Operation geheilte ungewöhnliche Lebercyste. *Prag med. Wchnschr.*, 17, 637, December, 1892
- ⁵ Beattie, D. A., and Robertson, H. D. *Lancet*, London, 2, 674, 1932
- ⁶ Bland-Sutton, J. *Brit. Med. Jour.*, 2, 1167, 1905
- ⁷ Borrmann, R. Zur Frage der cystischen Entartung der Leber. *Biblioth. Med.*, 13, 1, 1900
- ⁸ Boyd, Sidney. Nonparasitic Cyst of the Liver. *Lancet*, 1, 951, April, 1913
- ⁹ Burns, C. R. Case of Multiple Cystic Liver. *Jour. Path. and Bact.*, 28, 392, April, 1925
- ¹⁰ Cousins, J. W. Large Hepatic Cyst Simulating Ovarian Tumor. *Brit. Med. Jour.*, 11, 700, 1874
- ¹¹ Davis, C. R. Nonparasitic Cyst of Liver. *Am. Jour. Surg.*, 35, 590, March, 1937
- ¹² Eliason, E. L. Congenital Nonparasitic Cyst of Liver. *ANNALS OF SURGERY*, 99, 691, April, 1934
- ¹³ Harrington, S. W. *Surg. Clin. North America*, 6, 1191, 1926
- ¹⁴ Henke, F., and Lubarsch, O. *Handbuch der Speziellen Pathologischen Anatomie und Histologie*, Vol. V/1, 883
- ¹⁵ Jennings, W. K. Solitary Nonparasitic Cyst of Liver. *Surg.*, 6, 507, 1939
- ¹⁶ Jones, J. F. Removal of the Retention Cyst From the Liver. *ANNALS OF SURGERY*, 77, 68, 1923
- ¹⁷ Kaufmann, E. *Lehrbuch der speziellen pathologischen Anatomie*, ed. 6, 1, 608, 1911
- ¹⁸ Konjetzny, G. E. *Pathologische Anatomie und Physiologie der Gallenblasen und Gallengangserkrankungen*. *Ergeb. allg. Path. u. path. Anat.*, 14, 712, 1910
- ¹⁹ Lowenburgh, H. Congenital Unilocular Cyst of the Liver (Hemangioma). *Arch. Pediatrics*, 35, 285, May, 1918
- ²⁰ Maes, Urban. Nonparasitic Cysts of the Liver. Report of Two Cases. *Am. Jour. Surg.*, 38, 68, March, 1924

- ²¹ McCaughan, J H, and Rassieur, L J Transactions of Western Surgical Association, 1938
- ²² McGlannan, Alexius ANNALS OF SURGERY, 86, 844, 1928
- ²³ Montgomery, A H Solitary Nonparasitic Cysts of the Liver in Children Arch Surg, 41, 422, 1940
- ²⁴ Moschowitz, E Nonparasitic Cyst (Congenital) of the Liver With Study of Aberrant Bile Ducts A J M Sc, 131, 674, 1906
- ²⁵ Muto, Masao, and Hanzawa, Hogoro Zur Kenntnis der sogenannten solitären, waren Leberzyste Mitteilungen über allgemeine Pathologie und Pathologische Anatomie, 6, 153, 1930
- ²⁶ Neuwerk, C, and Hufschmid, K Über das multiloculare Adenokystom der Niere Beitr z path Anat u z allg Path, 12, 1, 1893
- ²⁷ Ochsner, E H Unilocular Cyst of Liver ANNALS OF SURGERY, 107, 829, May, 1938
- ²⁸ Orr, T G, and Thurston, J A Strangulated Nonparasitic Cyst of Liver ANNALS OF SURGERY, 86, 901, 1927
- ²⁹ Ottenheimer, E J, and Kinney, K Nonparasitic Cystic Disease of Liver New Eng J M, 200, 1093, May, 1929
- ³⁰ Parry, O K Congenital Cysts of the Liver J M Sc, New Jersey, 29, 560, July, 1932
- ³¹ Plenk, L Zur Kenntnis der solitären Leberzysten Virchows Arch f path, Anatomie, 201, 335, 1910
- ³² Sanger, M, and Klopp, A Zur anatomischen Kenntnis der angeborenen Bauchcysten Arch f Gynak, 16, 415, 1880
- ³³ Schaack, W Zur Frage der nicht parasitären Leberzysten Arch f klin Chir, 125, 183, 1923
- ³⁴ Shaw, H L K, and Elting, A W Congenital Cyst of Liver With Report of a Case Arch Pediatrics, 26, 818, November, 1909
- ³⁵ Siegmund, A Über eine cystische Geschwulst der Leber Virchows Arch f path Anat, 115, 155, 1889
- ³⁶ Sonntag, E Beitrag zur der Solitären nicht parasitarum Lebercysten Beitr z klin Chir, 86, 327, 1913
- ³⁷ Sternberg, C Pathologische Anatomie Ludwig Aschoff, ed 5, 1, 928, 1921
- ³⁸ Stoesser, A V, and Wangenstein, O H Solitary Nonparasitic Cysts of the Liver A J Dis of Children, 38, 241, August, 1929
- ³⁹ von Haberer, H Zur Frage der nichtparasitären Leberzysten Wien klin Wchnschr, 22, 1788, 1909
- ⁴⁰ von Kahliden, C Über die Genese der multilocularen Cystenmiere und der Cystenleber Beitr z path Anat u z allg Path, 13, 291, 1893
- ⁴¹ Wakeley, C P G, and MacMyn, D J Lancet, London, 2, 675, 1931
- ⁴² White, M Solitary Cyst of the Liver in a Child Age Four Months Arch Dis of Childhood, 11, 310, December, 1936
- ⁴³ Wikle, H T, and Charache, H Solitary Nonparasitic Cyst of the Liver A J Surg, 31, 345, February, 1936
- ⁴⁴ Witzel, O Hemicephalus mit grossen Lebercysten Cystenmeran, und einer Reihe anderer missbildungen Centrabi f Gynak, 4, 561, 1880

STUDIES ON THE USE OF METALS IN SURGERY*

PART II

EXPERIMENTS ON THE USE OF TICONIUM IN CRANIAL REPAIR

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IN A PREVIOUS COMMUNICATION¹ we have reported assays of cytotoxicity of certain metals in tissue cultures of chick embryo fibroblasts. Our purpose in that study, and in the present one, has been to find an alloy that conforms to the requirements of bone surgery and, hence, for the repair of cranial defects.

As was pointed out in that paper, an ideal cranioplastic substance should be nontoxic, strong and, at the same time, light enough to keep the bulk of the appliance small. In addition, it should be so malleable as to permit working and shaping during the operation. This latter characteristic is an exceedingly important one in cranial repair because casting is both time-consuming and expensive. For a cast plate to fit perfectly it is necessary to secure an impression of the defect itself. This is a cumbersome and often undesirable procedure to attempt at the time of operation. Many times the bone flap serves as a poor pattern either because it is diseased or the use of the rongeur has changed the shape of the defect after its removal. Estimation of the required plate by roentgenograms and measurement through the intact scalp is difficult. Finally, a cast plate, if found not to fit well, cannot easily be altered at the operating table.

The casting alloy Vitallium has been thoroughly studied by Venable, Stuck, and Beach^{2, 3, 4}. It is light, strong and nontoxic. It has been used for cranial repair by Geib,⁵ Peyton and Hall,⁶ and by Beck.⁷ Attention has been called to its lack of malleability as being undesirable. Its use in bone work in general, however, has been so satisfactory that we have used it as a control substance in our experiments, despite the fact that it does not completely fulfill the peculiar requirements for cranial repair.

The wrought alloy Ticonium is light and strong and, in addition, malleable. In the form of thin, perforated plates it can be cut with tin shears and molded by hand or with pliers. The perforations permit the making of slots or wedges to allow for unusual shapes, and provide many choices for screw holes.

Our previous study showed that wrought Ticonium and Vitallium and cast Ticonium (with beryllium), were not toxic to chick fibroblasts in tissue culture. The present paper reports results with these three alloys in repair of cranial defects in dogs. Some observations on electrolysis have been added.

* Read at the Annual Meeting of the Harvey Cushing Society in New York, N Y, May 21, 1942.

OBSERVATIONS ON DOGS

Method—Three different alloys were used Ticonium "wrought" (nickel 36.2%, cobalt 29.6%, chromium 28.2%, molybdenum 6%), Vitallium (cobalt 65%, chromium 30%, molybdenum 5%, manganese, silicon), and Ticonium "cast" (nickel 35.6%, cobalt 29.1%, chromium 27.7%, molybdenum 6%, beryllium 1.6%)

In Group I we used material prepared with the wrought alloy Ticonium* only This material consisted of sheets cold-rolled, with 30 per cent cold



FIG 1—(Dog 52)—"Wrought" Ticonium Plate over the temporoparietal region Eleven months after operation, showing the absence of corrosion of the metal Muscle overlying the plate and growing through the perforations has been reflected

reduction subsequent to the final anneal This seemed to be preferable for experimental purpose The plates had a thickness of 0.17 cm (27-gauge U S Standard) The sheets had been punched at intervals of 0.4 cm with holes 0.3 cm in diameter They were then polished, thus taking the punch marks out (Fig 1) Prepared in this manner, the plates were easily cut and molded at operation

The plates used in Groups II and III were cast in varying size and thickness, according to the shape of dogs' skulls Each plate had three attachments for the screws In most of the plates, four to five holes were punched A few solid plates were used In Group II, machine made screws of Vitallium,† and in Group III hand made screws of Ticonium "cast," were used

* The material made of Ticonium ("wrought" and "cast") was prepared by the Research Laboratories of the "Ticonium" Co, Albany, N Y

† The Vitallium plates and screws were furnished by the Austenal Laboratories, New York, N Y

Technic Healthy, well-nourished mongrel dogs of various ages were selected. The dogs were kept in separate cages and well fed. The animals were anesthetized by intra-peritoneal injection of nembutal (Abbott) (Max dose 0.7 cc of a 5 per cent solution per Kg body weight). The entire head or thigh was shaved and cleaned with a brush, soap, and water for a period of five minutes. Using strict aseptic technic, a unilateral U-shaped skin flap was turned down over the frontotemporoparietal region. The "temporal" muscle was sharply dissected from the underlying bone. The periosteum was scraped off, and, in the center of the denuded area of the bone, an opening was made by use of a trephine. This opening was enlarged to an average size of 2 x 3 cm. Throughout the procedure hemostasis was secured by use of the cautery. The dura remained closed with the exception of those experiments calling for the insertion of metal pieces into the cortex. In these instances a nick was made into the dura, the cortex was incised and a piece of metal about 0.2 x 0.3 cm was inserted vertically into the cerebrum.

In Group I a wrought Ticonium screen was used, having been previously autoclaved. From such a screen a plate was cut with tin shears to overlap the defect at all four margins by about 0.3 cm. This plate was then molded by hand to the convexity of the skull, and in each instance very satisfactory plastic repair was obtained. The plate was then fastened to the bone with 2-4 screws drilled into the bone to full length. Closure was performed in layers with the exclusive use of interrupted sutures of fine black silk. Skin closure was obtained with interrupted subcuticular sutures of the same material. A bandage dressing was applied and secured by an encasement of plaster of paris around the head and neck. The encasement remained in place for about five days.

Cast plates were used in the experiments of Group II and III. These plates, after having been autoclaved, were placed over the defect and fastened by screws drilled into the bone surrounding the defect.

Operations upon the femur were performed under the same aseptic conditions. A longitudinal incision was made over the lateral surface of the thigh. The muscles were bluntly dissected and retracted. The periosteum was removed, screw holes were drilled into the bone and the screws inserted. Closure was done in layers as above.

During the first postoperative day, fluids in the form of normal saline solution were administered subcutaneously. On the second postoperative day the dogs resumed their usual feeding. Body temperature was determined during the first postoperative days, and the dogs were reexamined at regular intervals. Roentgenograms were taken of a limited number of animals.

The dogs were sacrificed by intracardiac injection of ether or nembutal. Autopsy was performed, and the tissue fixed in 4 per cent neutral formaldehyde solution. Blocks were selected from the bone, and any grossly diseased viscera noted. These were embedded in paraffin or celloidin, and sectioned. Sections were studied with one or more of the following stains: Hematoxylin and eosin, Mallory's phosphotungstic acid hematoxylin, Masson's trichrome (Goldner's modification) and Giemsa.

GROUP I TICONIUM "WROUGHT"

Experimental Results—Twenty-one dogs were used for the experiments in this group. The tissues were exposed in all to a total of 115 pieces of metal. Fourteen plates, 78 screws in the skull bone, 19 screws in the femur and four pieces of metal which were embedded into the cerebral cortex. The dogs were observed from two days to 14 months, 17 animals were observed for a period of longer than 10 months. Fourteen dogs were sacrificed, and seven dogs died on account of secondary illness.

CASE REPORTS

Dog 25—*Operation* July 11, 1940. Plate secured with 2 screws. 7th post-operative day dog injured flap by scratching, secondary subcutaneous infection. Healed in 3 weeks. Sacrificed August 6, 1941.

Macroscopic Scar at operative site not unusual. Screws firmly embedded. Plate well attached, enclosed in a fibrous bursa-like sac. Metal shiny. No fluid. Bone defect filled by firm fibrous tissue.

to outer surface of which muscle is attached and grows through perforations in the plate Dura merges with this fibrous layer Underlying cortex normal

Microscopic Plate bed composed of smooth layer of laminated, partially hyalinized fibrous tissue Rare macrophage in looser connective tissue especially about blood vessels Some marginal new bone formation

Dog 36—*Operation* July 13, 1940 Plate secured with 4 screws Flap healed *per primam* 6th p o day semistuporous, drainage from eyes and nasal mucous membranes Slight motor weakness of both hind legs "Distemper" Died July 21, 1940

Macroscopic Operative site healing well Small hematoma in superficial fascial layer Surface of muscle overlying plate grayish brown Small amount of cloudy reddish fluid immediately about plate Screws secure Plate firmly attached Metal bright and shiny Dura underlying plate intact but dark red Not adherent to cortex Right side of heart dilated Lungs edematous Left kidney hydronephrotic

Microscopic Focal edema of lungs Chronic pyelonephritis Hyperemia of liver Cranial muscle focus of organizing fibrinous exudate and regenerating muscle Bone margin shows organizing fibrinous mat

Dog 38—*Operation* July 23, 1940 Metal inserted into cortex Plate secured with 4 screws Flap healed *per primam* Sacrificed September 4, 1941

Macroscopic Scar of operative site not unusual Screws firmly embedded Plate securely enclosed in bursa like sac Metal bright and shiny No fluid Bone defect bridged by firm fibrous layer, merging with dura Cerebral cortex surface adherent to dura over an embedded piece of bright, shiny metal which is surrounded by a thin white capsule

Microscopic Plate bed consists of laminated fibrous tissue At bone margin is considerable new bone almost bridging the gap Muscle fibers are oriented perpendicular to the plate bed No inflammation or necrosis Rare macrophage about blood vessels of muscle

Dog 40—*Operation* July 25, 1940 Plate secured with 4 screws Following day Fever, tachypnea, sputum (mixed bacteriae) Sulfapyridine Died after 30 hours

Macroscopic Generalized adiposity Skin flap flat and soft Fascia sutured tightly Plate firmly secured by 4 tightly embedded screws Metal smooth and shiny Between plate and dura thin layer of clotted blood Dura smooth and not adherent Dilatation of right side of heart Large foci of consolidation in lungs Uterus contains 2 small fetuses

Microscopic Obturation of bronchi by mucous and aspirated foreign material Massive atelectasis Thin layer of erythrocytes and fibrin above dura Small fibrinous clot in screw hole Muscle edematous, infiltrated with neutrophils (Period of observation too short Findings in accord with wound healing at this stage)

Dog 41—*Operation* July 26, 1940 Three screws inserted into frontoparietal region Three screws inserted into femur Scalp flap healed *per primam* Lower third of leg incision healed secondarily 15th p o day Sacrificed September, 1941

Macroscopic Operative sites show usual scarring Screws firmly embedded Metal shiny

Microscopic Skull screw hole lined by thin fibrous membrane immediately beneath which are rare macrophages containing pigment Loose fibrous tissue covers head Some laminated new bone beneath part of tract lining Femur screw hole essentially similar

Dog 42—*Operation* July 27, 1940 Three screws inserted into frontoparietal bone Flap healed *per primam* 12th p o day Fever, tachypnea Died August 13, 1940

Macroscopic Operative wound well healed Screws firmly embedded, have penetrated inner table Metal shiny No fluid Dura quite vascular Underlying cortex negative Dilatation of right chambers of heart Massive consolidation of lungs

Microscopic Necrotizing bronchopneumonia Screw holes, thin fibrous tissue lining with a few lymphocytes in vicinity Bone undergoing remodelling

Dog 43—*Operation* July 30, 1940 Metal inserted into cortex Plate secured with 4 screws Flap healed *per primam* Sacrificed August, 1941

Macroscopic Scar of operative site not unusual Plate firmly embedded in bursa like sac Screws secure Metal smooth and shiny Muscle has grown through perforations in plate Firm fibrous tissue bridges the bony defect and merges with the dura No adhesions to brain Piece of bright metal securely embedded in cerebral cortex and invested by a thin white capsule

Microscopic Brain Metal enclosed in a sac, inner lining of which is hyalinized collagen This is separated from brain by a thin, clear space containing a few macrophages several of which enclose black iron containing pigment The space is bounded externally by a poorly defined thin layer of disorderly gliosis Skull Screw holes and plate bed show usual fibrous tissue lining without inflammation or granulation tissue Rare pigmented macrophages in connective tissue especially about blood vessels

Dog 44—*Operation* July 31, 1940 Dura thickened and roughened Plate secured with 4 screws Flap healed *per primam* For 4 weeks dog continued to do well Exact data as to further course not available September 12th, dog was found dead

Macroscopic Animal emaciated, vomitus in mouth Scar of operative site not remarkable Plate firmly embedded in bursa like sac Metal smooth and shiny No fluid Bony defect filled by firm

fibrous tissue Small piece of shiny metal attached to dura by few adhesions Cortical surface not adherent Cecal diverticulum adherent and acutely inflamed

Microscopic Plate bed lining thin fibrous tissue layer No necrosis or inflammation

Dog 45 *Operation* August 2, 1940 Plate secured with 3 screws Flap healed without infection Dog did well until latter part of November Diarrhea, vomiting Died November 29, 1940

Macroscopic Plate and screws shiny Plate embedded in bursa like sac Bone defect filled by fibrous tissue Underlying brain negative Entire sigmoid edematous, hyperemic and ulcerated No peritonitis

Microscopic Colon Acute colitis with mucosal ulceration Skull Plate bed thin fibrous layer in which is some new bone formation partially bridging the defect

Dog 46—*Operation* August 2, 1940 Plate secured with 4 screws 3rd p o day papilledema on the right Disappeared after one week Skin flap healed *per primam* October 18, 1940, litter of eight puppies Low grade fever for 2 months, evidence of fatigue and exhaustion Impression "Low grade infection" Recovered by January, 1941 Clinically, remained well until sacrificed September 23, 1941

Macroscopic Skin and fascia at operative site appeared negative Muscle overlying the plate shaggy, soft, necrotic Cystic space between muscle and metal contained 4 cc of yellowish red serous fluid The usual fibrous sac about metal incomplete Metal smooth and shiny Three or 4 screws loose Bone defect replaced by firm fibrous layer with a rough surface Underlying cortex not adherent, grossly negative

Microscopic Brain Essentially negative Skull Plate bed composed of a thick layer of chronically inflamed granulation tissue in the inner layer of which are many neutrophils and eosinophils, acidophile necrotic masses are present in places along the lining The bony defect is bridged by dense fibrous tissue containing foci of new bone formation In this fibrous bridge are a number of small compact aggregates of lymphocytes and pigment bearing macrophages Bacterial stains reveal no organism

Dog 48—*Operation* August 7, 1940 Plate secured by 4 screws Flap healed *per primam* 20th p o day drainage from eyes and nasal mucous membranes Moist rales, right lung Despite sulfapyridine, progressive cachexia, loss of appetite, general weakness, fibrillary twitchings of muscles "Distemper" Died September 8, 1940

Macroscopic Plate and screws firmly attached Shiny and smooth Underlying dura merges with fibrous tissue layer, filling bone defect Focal pneumonia consolidation of lungs

Microscopic Lung Necrotizing pneumonia Skull Plate bed and screw hole lined by thin compact fibrous tissue layer Few pigmented macrophages

Dog 51—*Operation* August 6, 1940 Plate secured by 4 screws Post med screw not tight Post lat screw inserted obliquely Flap healed *per primam* 15th p o day diarrhea, progressive cachexia No clinical pulmonary findings Died August 27, 1940

Macroscopic Operative site insignificant Plate firmly embedded Screws secure except for post med screw which appears movable but in place Firm fibrous tissue bridges the defect and merges with the dura Underlying cortex not unusual Diffuse purulent bronchitis, with sparing of lower lobe of left lung Diffuse pneumonitis

Microscopic Skull Plate bed shows no sign of inflammation or necrosis

Dog 52—*Operation* August 8, 1940 Plate secured with 4 screws Post lat screw inserted obliquely Flap healed *per primam* Sacrificed September, 1941

Macroscopic Plate securely embedded in bursa like sac Screws firm Metal smooth and shiny Firm fibrous tissue bridges the defect in the bone and merges with the dura Underlying cortex not unusual

Microscopic Fibrous plate bed No inflammation or necrosis

Dog 55—*Operation* August 14, 1940 Plate secured by 4 screws Flap healed *per primam* Sacrificed September, 1941

Macroscopic Plate firmly embedded in bursa like sac Screws tight Metal smooth and shiny The bony defect is bridged by firm fibrous tissue which merges with the dura The underlying cortex does not show any gross changes

Microscopic Plate bed compact fibrous tissue with occasional macrophages in clefts and about blood vessels

Dog 56—*Operation* August 19, 1940 Four screws inserted in parieto occipital region Three screws inserted into femur Healed *per primam* Sacrificed September 25, 1941

Macroscopic Operative site insignificant All 7 screws firmly embedded Metal shiny No fluid

Microscopic Femur Screw tract lined by thin fibrous tissue Fine trabeculae of new bone aligned beneath part of tract lining In intervals where bone is deficient fibrous lining lies on fatty marrow Skull Screw holes lining shows no inflammation or necrosis

Dog 57—*Operation* August 23, 1940 Four screws inserted into frontoparietal region Four screws inserted into femur Healed *per primam* Sacrificed September 24, 1941

Macroscopic Operative scars grossly negative Eight screws firmly embedded Metal smooth and shiny

Microscopic Screw tracts in both bones show no inflammation or necrosis Thin fibrous layer

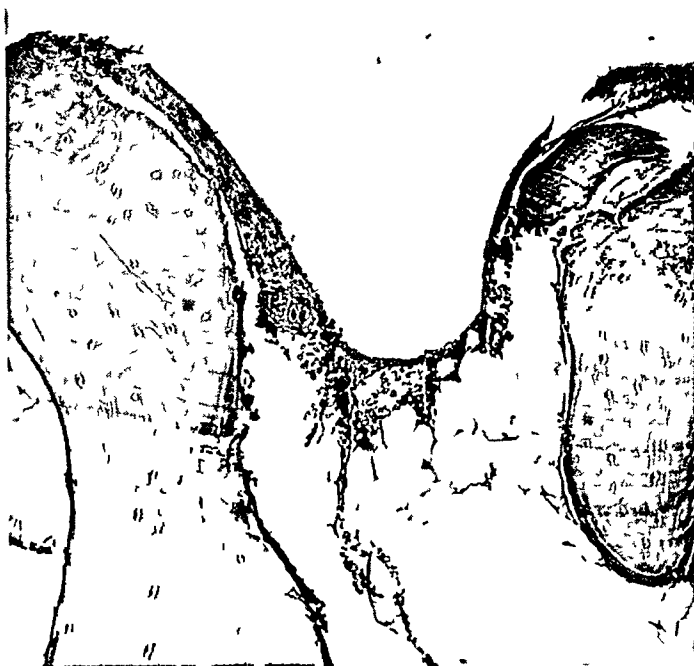


FIG. 2—(Dog 57)—“Wrought” Ticonium Screw hole in skull Eleven months after operation (H and E, $\times 170$)

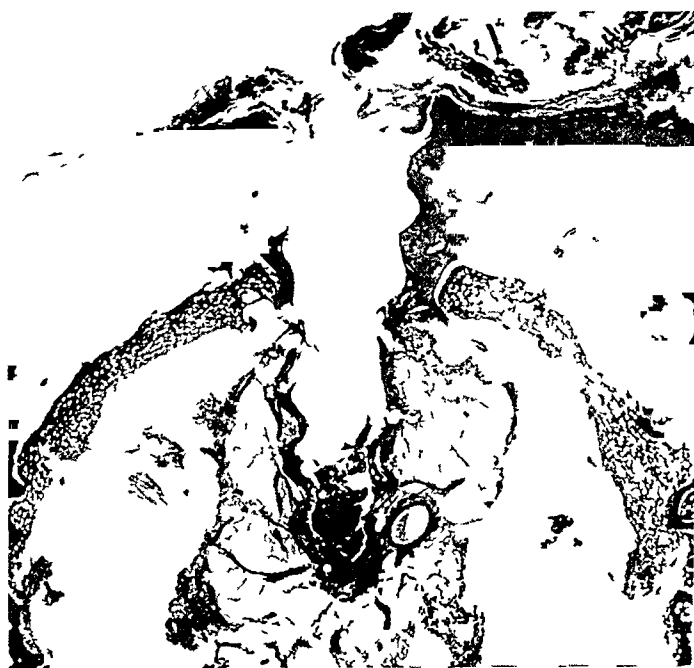


FIG. 3—(Dog 56)—“Wrought” Ticonium Screw hole in femur Eleven months after operation (H and E, $\times 14$)

over head of screws in skull and a spur of new bone is present in thickened periosteum of same region

Dog 58—*Operation* August 22, 1940 Four screws inserted into frontoparietal region Three screws inserted into femur Healed *per primam* Sacrificed September 1941

Macroscopic Operative scars not remarkable Screws firmly embedded Metal shiny

Microscopic Screw tracts lined by thin fibrous layer with rare pigmented macrophages nearby

Dog 64—*Operation* August 28, 1940 Plate secured with 4 screws Post lat screw not inserted in full length Flap healed *per primam* Sacrificed September 23, 1941

Macroscopic Operative scar not unusual Plate firmly enclosed in bursa like sac Screws tight Metal smooth and shiny Bony defect filled by fibrous layer Dura not adherent



FIG. 4—(Dog 43)—“Wrought” Ticonium Brain showing the tissue immediately adjacent to the embedded piece of metal Eleven months after operation (PTAH, $\times 170$)

Microscopic Plate bed consists of usual 3 layers of thin partly hyalinized collagen with rare pigment bearing macrophages in clefts about blood vessels No inflammation or necrosis

Dog 67—*Operation* August 20, 1940 Four screws inserted into frontoparietal region Three screws inserted into femur Healed *per primam* Sacrificed September 24, 1941

Macroscopic Operative scars not unusual Seven screws firmly embedded Metal smooth and shiny

Microscopic Screw tracts in both sites lined by thin fibrous tissue layer No inflammation No necrosis

Dog 68—*Operation* August 20, 1940 Dura vascular Dura opened Plate secured with 3 screws Flap healed *per primam* Sacrificed September 25, 1941

Macroscopic Operative site not unusual Plate firmly embedded into usual bursa like sac Screws tight Dura merges with fibrous tissue filling bone defect Underlying cortex negative

Microscopic Plate bed smooth thin compact fibrous layer with slight new bone formation in bony defect Rare pigmented macrophage

Dog 70—*Operation* August 31, 1940 Four screws inserted into frontoparietal region Three screws inserted into femur Flap healed *per primam* Sacrificed September, 1941

Macroscopic Operative scars not significant All screws firmly imbedded, shiny

Microscopic Screw tracts in both bones have thin fibrous linings resting on fat & marrow or spicules of newly formed bone Some periosteal new bone also formed around screw point in skull where it has passed through internal table

COMMENT All screws and plates in this series were securely fixed and showed no corrosion

In the presence of a wrought Ticonium plate, skull defects underwent uncomplicated repair. Two layers of parallel hyalinized fibers were laid down continuous with the pericranium and dura, respectively, the pericranial layer being somewhat thicker. Between these two layers was a third, the new fibers of which were deposited parallel to the surface but at right angles to those of the other two. The larger blood vessels coursed in this middle layer. A limited amount of periosteal new bone was formed which failed to fill the gap. The bone margins underwent remodelling so that they were smooth and tapered in cross-section. Small tufts of muscle filled the plate perforations. Screw holes were lined by a thin layer of fibrous tissue with fibrils again parallel to the metal surface. This lining lay on a base composed of either new bone spicules or fatty marrow (Figs 2 and 3).

The tissue about metal implants in the brain showed only a thin layer of fibrous tissue beneath which were a few macrophages. The brain substance proper showed a narrow zone of gliosis. The vessels appeared negative (Fig 4).

A single exception to the otherwise uniform results was found in Dog 46. Necrosis and polymorphonuclear cell exudate characterized the tissue response. This was unique in this group, which included 21 dogs and 115 pieces of metal. The reaction in this case could be differentiated, histologically, from the toxic response seen in Group III. We could not, however, differentiate between Dog 46 and one infected case in Group III. The clinical history and the pathologic findings, as noted in the protocol, suggested infection.

In many cases, a dark brownish or black pigment containing iron was present in macrophages. These were found in clefts between the fibrous tissue of the skull defects just beneath the fibrous lining of screw holes and in the muscle about the screw heads. The macrophages were most numerous about blood vessels but could not be found immediately adjacent to the metal. The amount of pigment was small, never constituting granulomata. It appeared to be identical with the pigment seen about Vitallium plates and screws.

It may be concluded, therefore, that wrought Ticonium is essentially inert, as is Vitallium.

GROUP II VITALLIUM

This alloy was examined in seven dogs. The tissues were exposed in all to a total of 34 pieces of metals, three plates and 31 screws. The animals were observed from 24 days to 15 months. Five dogs were sacrificed, and two died on account of secondary illness.

CASE REPORTS

Dog 6—*Operation* December 1, 1939. Plate secured with 3 screws. Secondary subcutaneous infection in area about medial flap margin. Healed 26th p.o. day. Sacrificed September 3, 1940.

Macroscopic Skin scar sound. Muscle tufts have grown through perforations in plate. Screws tight. Plate firm. Metal smooth, and shiny. Dura thickened but not adherent to cortex.

Microscopic Plate base consists of hyalinized fibrous tissue merging with bone. At the margin

of the two tissues are a few spicules of new bone arising from periosteum. Very rare macrophage in fibrous tissue clefts contains iron pigment.

Dog 13—Operation December 29, 1939. Plate secured with 3 screws. Healed *per primam*. Sacrificed September 3, 1940.

Macroscopic Skin scar negative. Plate and screws tight. Muscle has grown through plate perforations. Metal smooth and shiny. Dura thickened beneath the defect but not adherent to cortex.

Microscopic Defect filled with bridge of hyalinized fibrous tissue merging with bone. In clefts of fibrous tissue iron-containing pigment in macrophages. Muscle attached to plate bed appears negative. Some foreign body response to bone wax.

Dog 16—Operation February 15, 1940. Solid plate secured with 3 screws. Posterior screw not tight. Flap healed *per primam*. Sacrificed September 3, 1940.

Macroscopic Skin scar sound. Screws firm. Plate shiny and well fixed. Underlying dura thickened but not adherent to cortex.

Microscopic Defect bridged by laminated, partly hyalinized fibrous tissue. Between a few fibers, especially near vessels, are occasionally pigment-bearing macrophages. Slight new bone formation.

Dog 30—Operation June 29, 1940. Six screws inserted into frontoparietal region. Due to injury, flap broke open. Secondary subcutaneous purulent infection. Healed 20th post-operative day. Sacrificed September 23, 1941.

Macroscopic Scar and musculature negative. All 6 screws firmly embedded, smooth and shiny.

Microscopic Screw tract lined by thin fibrous layer, with fibers parallel to screw surface. This rests on spicules of new bone or on fatty marrow. Considerable periosteal new bone at dural end of tract, where screw has evidently penetrated inner table pushing periosteum before it. Few pigment-laden macrophages in looser connective tissue just beneath fibrous lining. Same type of macrophages in connective tissue about head of screw. Here, they seem chiefly perivascular.

Dog 31—Operation June 30, 1940. Six screws inserted into frontoparietal region. All screw holes somewhat too large. Flap healed *per primam* 26th post-operative day, drainage from eyes and nasal mucous membranes. Slow and incomplete recovery. Two months later flaccid paralysis of both hind legs. Epileptic seizures. "Distemper." Died December 19, 1940.

Macroscopic Operative scar negative. Six screws firm.

Microscopic Screw tract lined with thin laminated fibrous tissue. Occasional pigment-laden macrophage in looser tissue immediately adjacent.

Dog 32—Operation July 6, 1940. Six screws inserted into frontoparietal region. Flap healed *per primam* 5th post-operative day, drainage from eyes and nasal mucous membranes, fever, dyspnea. "Distemper." Died August 1, 1940.

Macroscopic Operative scar insignificant. Muscle grossly negative. Six screws firm and shiny. All 6 screws have passed through the inner table. Appear as firm smooth nodules on dural sides. Not adherent to cortex. Right atrium and ventricle of heart dilated. Lungs consolidated.

Microscopic Screw tract lined with thin fibrous tissue layer. Considerable periosteal new bone formed at dural end of tract. Rare pigment-bearing macrophage.

Dog 34—Operation July 10, 1940. Four screws inserted into frontoparietal region. Flap healed *per primam*. Sacrificed September 23, 1940.

Macroscopic Muscle and skin of operative site negative. Four screws firm. Metal smooth and shiny. Dura smooth.

Microscopic Slight new bone formation between dura and inner table near point of screw. No reaction in tract.

COMMENT—The original purpose of using Vitalium in these experiments was chiefly to supply a control series. These results are reported merely to confirm the histologic studies of Venable, Stuck, and Beech^{2, 3}. They are of particular interest only in that a longer observation and survival period is covered than yet recorded.

In brief, no evidence of toxicity was found. The screws were tight, the plates firmly fixed, and the metal shiny. Cranial defects healed normally, and the tissues on which the plate rested showed no necrosis nor inflammation. The screw holes were lined by a thin layer of fibrous tissue overlying newly formed trabeculae of bone or fatty marrow (Fig. 5).

In every case an occasional pigment-bearing macrophage in the vicinity of the metal was observed. These cells were located in spaces between collagen fibers in the skull defects and about blood vessels. In screw hole tracts they were usually seen beneath the thin fibrous inner lining, and here, too,

were often clustered about vessels. They were not noted immediately adjacent to the metal. This pigment contained iron and it is presumed to be the same as that reported by Wise⁹ about a Vitallium Smith-Petersen nail. It is worthy of note that this pigment occurred in very small amounts, that it did not give rise to granulomata and in our opinion does not constitute a sign of toxicity. As was noted above this pigment was also found in



FIG. 5—(Dog 30)—Vitallium Screw hole in skull. Fourteen months after operation. (H and E, X170)

animals in which Ticonium "wrought" was buried. Since both Vitallium and wrought Ticonium are nonferrous alloys, the iron cannot have been derived from these metals. Our data do not permit us to assign its source. We are inclined to agree with Wise that it is of hematogenous origin.

GROUP III TICONIUM 'CAST' WITH BERYLLIUM

This alloy was tested in 14 animals. The tissues were exposed to a total of 55 pieces of metals. Nine plates, 35 screws in the skull bone, 10 screws in the femur, and one piece of metal which was embedded into the cerebral cortex. The dogs were observed from 50 days to 22 months. Eight animals were observed for a period longer than 10 months. Eleven dogs were sacrificed, three died on account of secondary illness.

COMMENT—The findings in this group may be summarized without giving the individual case reports of the 14 animals observed.

In dogs which were killed before six months plates were firmly fixed, screws were tight and the metal was bright and shiny. In dogs which survived longer, however, screws were usually loose and the tissues about the plates were discolored. Occasionally fluid was found about the metal.

Histologically the screw holes and plate beds were lined by chronically inflamed granulation tissue containing many macrophages. In the vicinity of the screw holes there was extensive fibrosis of the marrow and some

new bone formation. In general, the amount of lymphocytic and macrophagic exudate was greater in long term experiments. In one dog which survived three months the plate bed consisted of dense fibrous tissue in which were a few focal collections of lymphocytes and macrophages especially numerous about the plate edge. In another dog which survived 22 months, the lining of the space filled by the plate consisted of macrophages with their long axis perpendicular to the plate surface so that these formed a palisade-like layer. The tissue beneath them was highly vascularized and great numbers of swollen macrophages and lymphocytes were enmeshed in a loose fibrillar network. There was a thick layer of fibrous tissue, partly hyalinized beneath the granulations. In the interstices of this were foci of lymphocytic infiltration. Similar changes were seen in the brain where a thick fibrous capsule was surrounded by degenerated brain substance markedly infiltrated with lymphocytes. Perivascular lymphocytic collars were present at some distance from the metal. In spite of the extensive exudative reaction fibroplasia and osteoplasia were not significantly impaired. In the skull periosteal new bone formed near the bony margin of the defects. In femurs the usual fine trabeculae of the marrow were replaced, in the vicinity of the screws by dense bone having well developed Haversian systems.

These observations are at variance with the results obtained in fibroblast cultures. Two explanations suggest themselves. The first is that the time during which a metal may be studied in any one generation of fibroblasts *in vitro*, is insufficient. Against this explanation is the unimpaired fibroplasia in the long term *in vivo* experiments. The second is that a factor of *selective cytotoxicity* complicates the picture. By this it is meant that some metals may not be toxic to fibroblasts although they may be toxic to other types of cells.

Whatever the explanation, Menegaux's⁸ belief that fibroblast cultures are a valid medium for testing all metals may be questioned.

OBSERVATIONS ON ELECTROLYSIS

Venable, Stuck and coworkers^{2, 3, 4} maintain that electrolysis is the controlling factor in osteosynthesis with metals, and that "metals which are nonelectrolytic in body fluids cause no pathologic reaction in the tissue." This has been a point of controversy. Murray, Martin¹⁰ (Fracture Committee of the American College of Surgeons, New York, 1938) and Key¹¹ do not feel that electrolysis has an essential bearing on the problem. Bothe, Beaton, and Davenport^{12, 13} concluded that "electrolysis is an accompaniment of unfavorable bone reaction rather than the direct cause of it."

Using Venable's method, we have checked the electrolytic activity of the two Ticonium alloys and compared them with that of Vitallium and Vanadium. Silver and copper were used as anodes. Ringer's solution served as electrolyte. A micro-ammeter with an internal resistance of 50 ohms was used. Full-scale deflection amounted to 120 micro-amps. The results are given in Table I.

It is of interest to note that the final reading for Ticonium 'wrought' and Vitallium approximates zero, while Ticonium 'cast' shows only a minimum current. Ticonium "cast" did not prove to be toxic to fibroblast cultures but did give a local toxic response in dogs which was out of all proportion to the minimal galvanic current produced.

It is common knowledge that pure copper is toxic by chemical action even though it cannot be accused of being electrolytic. This may be taken to indicate that electrolysis may be an accompanying factor of unfavorable bone reaction but it cannot be its only cause. Key has presented good evidence as to its lack of importance clinically.

TABLE I
ELECTROLYTIC DETERMINATIONS

Cells in Ringer's Solution	Initial Deflection in Micro amperes	Immediate Drop in Micro amperes to	Deflection after 3 Minutes in Micro amperes	Deflection after 90 Minutes in Micro amperes
Ticonium wrought copper	24	3	0	0
Ticonium wrought -silver	24	3	0	0
Vitallium copper	35	2½	0	0
Vitallium silver	35	2½	0	0
Ticonium cast copper	100	24	15	0
Ticonium cast -silver	100	24	13	0
Vanadium copper	' off scale	—	—	' off scale
Vanadium silver	off scale	—	—	' off scale

The data recorded in this table were compiled by Mr. L. Griffith, Chief Metallurgist, Research Laboratories, Ticonium Co., Albany, N. Y.

Discussion—Our observations as expressed in the present communication, establish the inertness in tissues of wrought Ticonium and Vitallium.

Contrary to our previous conception, the cast alloy Ticonium (containing beryllium) proved to be toxic *in vivo**. It did not, however, interfere with fibroplasia or osteoplasia in any of the animals observed. Therefore, it seems unlikely that the short duration of the tissue culture experiment is the explanation for the lack of 'fibroblast cytotoxicity'. The evidence is in favor of a *selective cytotoxicity* of the toxic agent, which presumably in this case is beryllium.

Our experiments to date lead us to believe that fibroblast cultures and electrolytic measurements are inferior to histologic studies as tests for the toxicity of metals.

In the alloy Ticonium "wrought" (*without* beryllium), it is believed that a material has been found which conforms to the requirements set forth for the use of metals in the repair of cranial defects. Accordingly, we have commenced to use this alloy as cranioplastic material in patients and will report our observations at a later date.

* Ticonium is made in several forms, "wrought" Ticonium for surgical purposes and a cast form with beryllium for dental restorations. As employed in the dental alloy beryllium, we are informed, improves the casting qualities of Ticonium and assists the production of appliances of extreme dimensional accuracy. It has been used successfully in dentistry for some years. Surgical appliances are not made of cast Ticonium with beryllium. While this alloy is toxic *in vivo*, no interference can be drawn from our experience and information on its behavior in such external appliances as dental restorations.

SUMMARY

1 The alloys Ticonium "wrought" Vitalium, and Ticonium "cast," have been studied *in vivo* with special reference to their usage as cranioplastic material

2 Ticonium "wrought" and Vitalium have been found inert Ticonium "cast" (with beryllium) has been found cytotoxic It is suggested that this toxicity is "selective"

3 Fibroblast cultures and electrolytic measurements have been found inferior to histologic studies as tests for the toxicity of metals

4 The importance of carrying out *in vivo* studies for periods longer than six months is indicated by the late toxic reaction in the Ticonium "cast" material

5 The wrought alloy Ticonium appears worthy of trial as a cranioplastic material in man

The authors wish to express their appreciation to Drs B Williams and T Engster for their assistance, and to Mr E Touceda and Mr E Griffith for their advice in the metallurgic phases of the study

REFERENCES

- ¹ Campbell, E, Menowsky, A, and Hyde, G Studies on the Use of Metals in Surgery Part I Comparative Determinations of the Cytotoxicity of Certain Metals in Fibroblast Culture ANNALS OF SURGERY, 114, 472-479, 1941
- ² Venable, C S, Stuck, W G and Beach, A The Effects on Bone of the Presence of Metals, Based upon Electrolysis Jour South Surg Assn, 49, 294-315, 1937
- ³ Venable, C S Osteosynthesis in the Presence of Metals Jour South Med Assn, 31, 5, 1938
- ⁴ Venable, C S, Stuck, W G Three Years Experience with Vitalium in Bone Surgery ANNALS OF SURGERY, 114, 309-315, 1941
- ⁵ Geib, F W Vitalium Skull Plates JAMA, 117, 8-12, July, 1941
- ⁶ Peyton, Hall The Repair of a Cranial Defect with a Vitalium Plate Surgery, 10, 710-716, 1941
- ⁷ Beck, Claude Repair of Defects in Skull by Ready Made Vitalium Plates JAMA, 118, 798-799, 1942
- ⁸ Menegaux, G Influence des metaux couples, sur la croissance des cultures *in vitro* de fibroblastes et d'osteoblastes Compt rend Soc de biol, 119, 485-487, 1935
- ⁹ Wise, R A Histological Study of a Transcervical Fracture of the Femur after Internal Fixation Jour Bone and Joint Surg 23, 941-947, 1941
- ¹⁰ Crowell, B C Report of Symposium on Metallic Fixation in Fracture S G & O, 68, 576-578 1939
- ¹¹ Key, J A Stainless Steel and Vitalium in Internal Fixation of Bone A Comparison Arch Surg, 43, 6-5-626 1941
- ¹² Bothe, R T, Beaton, L E, and Davenport, H A Reaction of Bone to Multiple Metallic Implants S G & O, 71, 598-602, 1940
- ¹³ Bothe, R T, Davenport, H A Reaction of Bone to Metals II Lack of Correlation with Electric Potentials S G & O, 74, 231-235, 1942

THE USE OF A LAMP TO WARM MOIST COMPRESSES*

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HOW TO KEEP COMPRESSES HOT is a perennial question on any surgical service. Its answer interests the nurse, administrator and surgeon, for practical technic, hospital costs and effective therapy are involved. The control of temperature probably influences the rate of healing of any wound but is especially important in lesions of an extremity having an impaired circulation for here uncontrolled heat may cause harm.

Compresses are usually kept at a higher temperature than the surrounding air, so some external source of heat must be provided to counteract the normal heat loss. The five methods of supplying heat that have been used are (1) The repeated application of a hot solution or frequent changes of hot dressings (2) A poultice (3) Hot water bottles (4) An electric heating pad (5) Radiant heat from a lamp. The repeated application of a hot solution or hot dressings is inefficient because of rapid cooling, after which the compress becomes cold and clammy. The preparation of a poultice is rapidly becoming a lost art and, though those prepared by some older nurses appeared to do good, yet one hesitates to order them at present for fear of the result. Hot water bottles are safe and, if covered with a rubber sheet and blankets to prevent heat loss, are effective. They have the disadvantages of causing pain in an infected wound from the weight of the bulky dressing and of requiring excessive nursing time to keep them warm. Electric pads would appear to be satisfactory, but the usual ones cannot be relied upon to maintain a constant temperature so are a source of trouble and worry. A satisfactory heating element can be manufactured at a moderate cost, but a good rheostat cannot be made for the price obtained for most electric pads. The use of an accurate rheostat has been tried but it increased the cost beyond the salability of the product and was discontinued. Cooley[†] has described an excellent electric heating unit designed for compresses. It has an accurate, controllable rheostat but this very fact makes it expensive for the average institution to purchase the number required for an active surgical service.

Lights or baking lamps have long been used in treatment and Dr. Stafford Warren[†] and I thought radiant heat from this source would be the cheapest, safest and most effective means of heating compresses. The only question to be settled was how it could best be applied. A bed cradle, with lights controlled by a rheostat, will maintain a fairly constant temperature but it is awkward and bulky for routine use on compresses. The portable baker

* This study received assistance from the Siever's Fund.

† Doctor Warren first interested me in the use of radiant heat when I had an infected hand and could judge subjectively the effect of various compresses. I am indebted to him for advice during these observations.

used in physiotherapy gives a concentrated heat to a limited area. It has two drawbacks for unrestricted use. First, high initial cost, and, second, danger from burns. The "therapy" or "baking" lamp is easy to regulate, cheap, and compact, so appeared to be the best means of supplying the radiant heat to compresses.

The construction of such lamps is fairly uniform, most of them having an aluminum reflector with either a tungsten bulb or a silicon-carbon heating element. They vary in design, and in their external frame, for there are "floor" models, "table" models and "hand" or bracket lamps. None of these commercial types were suited for our purpose. The "floor" model with a round base was unstable and would tip over, while that with a tripod base was cumbersome to have at the bedside since the legs stuck out and the attendants tripped over them. The "table" model has a very small base which made it so unstable that it was dangerous. If one of these hot lamps fell onto a patient it would cause a severe burn, so that a rigid attachment was considered obligatory, it being better than insurance.

Hand lamps with a spun aluminum reflector and tungsten bulbs were purchased for \$2.48 each, and stripped of their handles. A $\frac{1}{4}$ " rod, 18" long, was welded to the ball and socket joint of the bracket and fastened by a laboratory clamp holder to a $\frac{3}{8}$ -inch upright rod, 36 inches long. This upright rod was fastened to a specially machined bracket which clamped onto the frame of the bedspring (Fig. 1). This bracket allowed adjustment of the lamp to any point from the head to the foot of the bed, while the laboratory clamp connecting the vertical and horizontal rods gave adjustment in rotation up and down, or across the bed, yet, once it was tightened in place the whole apparatus was rigid and secure, being free from the danger of falling on the patient. This arrangement was cheap (total cost \$7.50 per unit), compact, and appeared satisfactory, but when it was put to use an unexpected difficulty arose from variation in bedspring construction. It was found that in this hospital alone there were five different kinds of bed springs! These were of two general types, one with the angle-iron of the frame turned up and the other turned down, so, with minor adjustments two types of the bracket could be made to serve (Fig. 2).

In an effort to construct an attachment suitable for all beds the idea of clamping the lamp to the spring was discarded in favor of attaching it to a rod which was clamped to the head and foot of the bed (Fig. 3). The lamp assembly was mounted on a sleeve which slid on a piece of pipe-conduit attached to the ends of the bed. For ease of attachment a hook was put on the head-end to hold it in place, while the screw was tightened at the foot. This apparatus cost about \$10.00, when made in our shop. It was a little unwieldy to carry about the hospital but other than this, has been satisfactory.

NURSING METHOD

The routine use of these lights for compresses is as follows:

- (a) The bed is protected with a rubber sheet

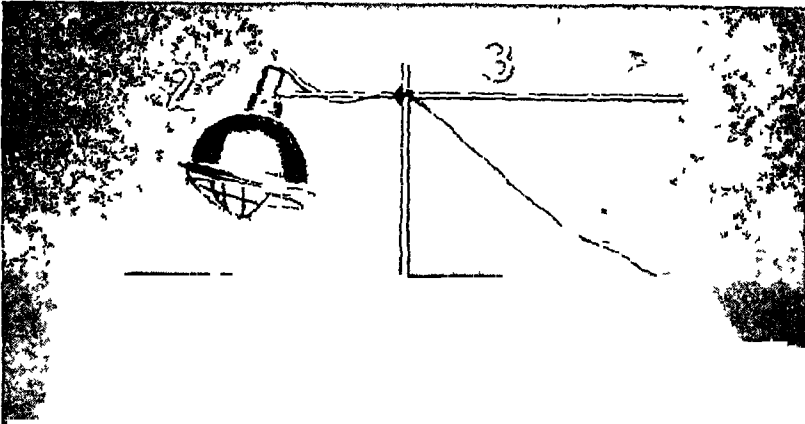


FIG 1—The compress light which attaches to the bed (1) Shows one type of the machined clamp which attaches to the angle iron of the bed spring to hold the vertical 36" rod (2) Is the lamp which has the ball and socket joint of its original bracket welded to a horizontal rod 18" long (3) Shows the attachment of the horizontal rod to the vertical rod by a laboratory clamp holder, which gives vertical, horizontal, and rotary motion

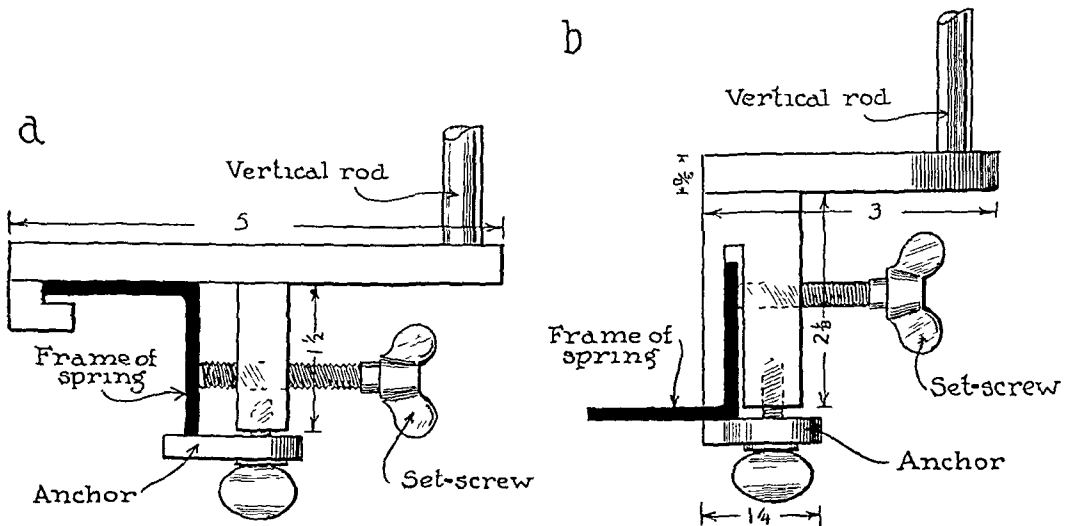


FIG 2—Construction details of the two types of clamps to fasten the vertical rod to the bed spring (a) Shows the clamp for use when the angle iron of the frame turns down. Adjustment is provided for $1\frac{1}{4}$ " and $1\frac{3}{4}$ " angle iron. The button or "anchor" at the bottom was found to add to the stability (b) Illustrates the clamp designed for a frame with the angle iron turned up. The slot slips over the frame and is held with a set screw. Here, also, adjustment is provided for variation in the size and thickness of the frame



FIG 3—Attachment of the lamp to a pipe which is clamped to the head and foot of the bed. In the lower illustration (1) is a clamp tightened by a screw that threads on a nut inside the conduit. This screw is 12" long to allow adjustment for beds that vary in length from 6'6" to 7'4" (2) Is a sleeve that slides along the pipe to the head or foot of the bed. It carries a vertical rod 36" long, which has a slight outward bend at its base to clear the mattress. (3) Is a hook to catch on the cross bar of the head of the bed to hold this clamp while the other end is tightened. It was originally made with two hooks, to be interchangeable on the two sides of the bed. (4) Is a sleeve that fastens on the vertical rod and carries the horizontal rod. This raises, lowers, or rotates the lamp. (5) Is a sleeve which allows movement in a horizontal plane or permits tilting the lamp.

- (b) The wound is dressed with two layers of moist gauze covered with oiled silk
- (c) This dressing is covered or wrapped with a sterile towel
- (d) A bath thermometer is placed near the wound
- (e) The light is centered on the wound and raised or lowered until the thermometer reads 110° F
- (f) Unprotected skin near the lamp may be covered with a towel to prevent discomfort
- (g) Drafts near the lamp are avoided
- (h) Compresses are moistened every three hours

The temperature beside the wound may be from 5° to 10° F lower than that of the bath thermometer outside the compress

RESULTS

After using these lamps for a year, it has been observed that when moist compresses are used the nurses prefer the lamp because it takes less work, the patients like it because it is comfortable and the surgeon orders it because it is effective. However, these opinions are partially subjective so it was desired to obtain quantitative information on the temperature control and nursing time with the various types of compresses.

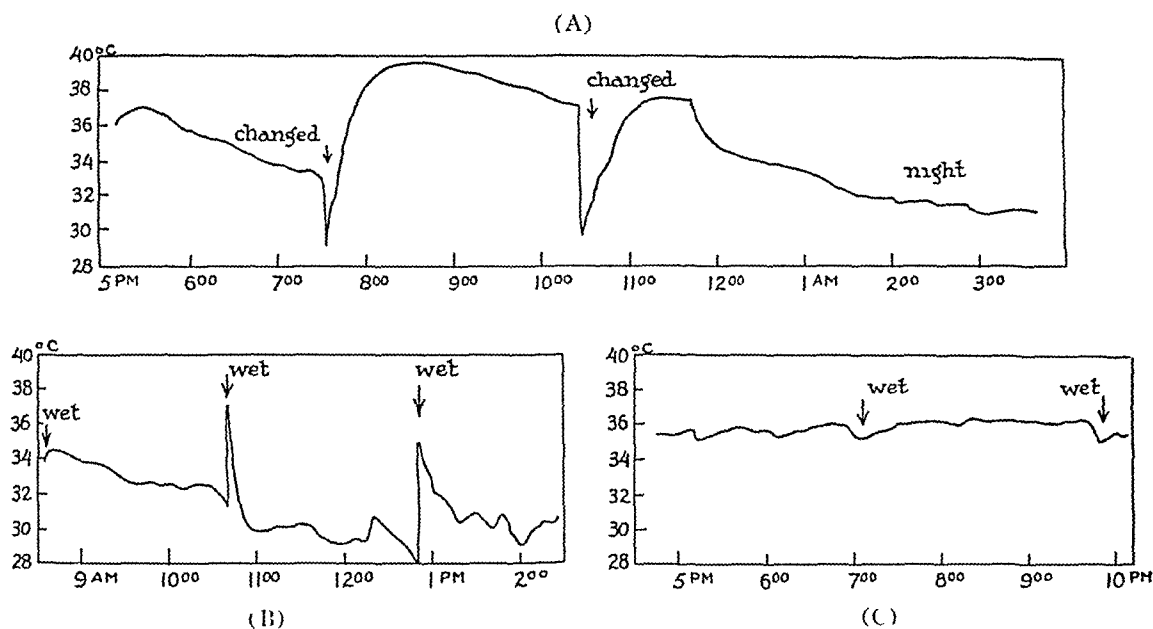
The temperature was obtained by means of an electrode separated from the wound by one layer of gauze. This electrode was attached to a continuous temperature recording device loaned to me by Mr. Bishop. Typical graphs are shown in Graph 1, where it will be seen that only with the light is a continuous elevation of temperature maintained. This has also been observed by Cochran.¹ The "massive compress" consists of moist gauze covered by oiled silk, wrapped with a Turkish towel, which has several hot water bottles outside it. These are covered with a rubber sheet, and the whole is wrapped in a blanket which is pinned tightly in place from the tip to the base of the limb. With all this, the temperature is found to fall after about an hour (Graph 1A). Dressings which are moistened periodically with a warm solution (Graph 1B) are found to cool in 10 or 15 minutes to room temperature. Compresses warmed with a lamp fluctuated in temperature only if the patient's bed was in a draft.

Computation of nursing time for the care of different compresses gave interesting results. The head nurses kept an accurate record of the time consumed with the different procedures. The "massive compresses" required an average of four hours a day, per patient, or 28 hours a week. The moist compresses, kept warm by a lamp, required an average of 40 minutes a day or 4.66 hours a week, or a saving of 23.33 hours a week of nursing time per patient. If nursing time is considered to cost an average of 60 cents per hour, then the "massive compress" costs the hospital \$16.80 per patient per week for nursing, while the compress and light cost \$2.80 or a saving of \$14.00 per patient week. The added cost of the electric current used for the lamp about equalled the cost of the added dressings used in the massive compress. The amount saved in nursing time in one week on

one patient was more than the initial cost of the lamp so the administration of the hospital was very willing to buy all the lamps that were needed

This study brought up a question that was not satisfactorily answered—"What is the optimum temperature for the healing of a wound?" We know that the normal vasodilatation level is between 31° and 33° C. We also

CONTINUOUS TEMPERATURE READINGS ON MOIST COMPRESSES



GRAPH 1—Continuous temperature readings on moist compresses (A) "Massive" compresses—Nursing time, four hours a day. The temperature is maintained for about an hour and then begins to fall. They are changed every three hours. (B) "Moist" dressings without external source of heat. Moistened every three hours. Nursing time, 40 minutes a day. The heat is retained for only 10 or 15 minutes. (C) "Moist" dressings with light as source of heat. Moistened every three hours. Nursing time, 40 minutes a day. A constant, effective temperature is maintained.

know that in peripheral vascular disease this level is as low as 23° or 24° C, and that overheating such an extremity accumulates waste products from local tissue metabolism which damages the tissue. This demands exact control of the external temperature with an impaired circulation. But with a normal blood supply it is possible that the rate of healing of wounds can be accelerated by temperatures in excess of the normal vasodilatation level. This should be determined, for it is pertinent.

SUMMARY

Warm, moist compresses are a satisfactory means of treating open, infected or granulating wounds. For this purpose, a source of external heat must be provided. A baking lamp was found to maintain a constant temperature, to eliminate the bulk and weight of a large dressing and to save nursing time. One year's experience has shown it to be safe and effective.

Clamps to attach these lamps to the bed have been designed and are described.

REFERENCES

- ¹ Cochran, J. R., Jr. An Improved Method of Applying Moist Heat to Infected Extremities. *Jour. Am. Med. Assn.*, 112, 2039, 1939.
- ² Cooley, K. L. A New Apparatus for Maintaining Hot Compresses at Constant Temperature. *Arch. Surg.*, 37, 123, 1938.
- ³ Morton, J. J., and Scott, W. J. M. The Measurement of Sympathetic Vasoconstrictor Activity in the Lower Extremities. *Jour. Clin. Investigation*, 9, 235, 1930.

THE ANATOMIC APPROACH TO PULMONARY RESECTION

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INDIVIDUAL LIGATION of the pulmonary vessels and careful suture of the bronchus in the performance of complete unilateral pulmonary resection has received preference over other measures for several years. This method was popularized by Rienhoff,¹ Crafoord,² Mason³ and others and the results have been so satisfactory that few will resort to tourniquet control of the

FIG. 1. A

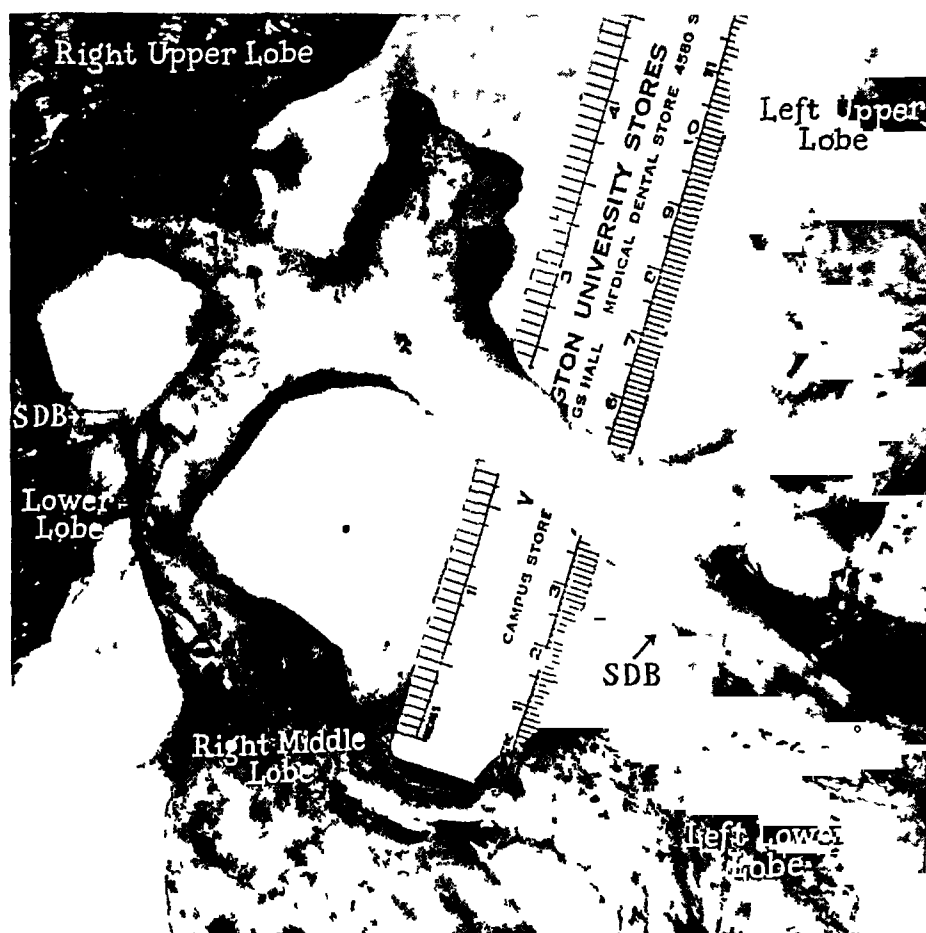


FIG. 1. A—Dissected specimen showing bronchial divisions of greatest surgical importance. Note branch bronchus to superior divisions of the lower lobes (SDB).

hilum or to mass ligation except in those instances in which individual dissection of the pulmonary veins, the pulmonary artery and the bronchus are impossible or unwise because of existing circumstances. More recently, efforts have been made to apply the principle of separate ligation and suture to partial pulmonary resection by ourselves^{4, 5} and by Churchill^{6, 7}. Here again, the preliminary results have been so promising that the technic will, in our opinion, replace all other methods save in those cases in which it cannot be employed because of technical or other reasons.

Combined clinical experiences and investigatory observations have yielded certain facts of anatomic importance which we consider worth making a part of the record. The comprehensive picture of the surgical anatomy of pulmonary resection may be assembled upon our conception of the tracheobronchial tree. In addition, the management of the bronchial stump after pulmonary resection is so important that the anatomic characteristics of the bronchial tree are secondary to no other considerations.

FIG 1 B



FIG 1 B—Another specimen showing similar pattern of the bronchial tree. This is the configuration usually encountered.

Figure 1, A and B, are photographs of dissections of lung specimens made to demonstrate the surgical anatomy of the bronchial tree. An understanding of these structures is important, whether it is to be applied to total unilateral or to partial pulmonary resection. The similarity of the specimens is striking and characteristic. It can be seen that the left main bronchus is so long that it offers more than adequate proportions for amputation and complete closure of the stump except in those instances in which it is necessary to divide the bronchus at the trachea. On the right side, the main bronchus is shorter, due to the point of origin of the upper lobe bronchus. Indeed, it is true that the upper lobe bronchus sometimes arises at a much higher level than shown in the illustration, and, occasionally even from the wall

of the trachea. In general, however, the main bronchi are entirely adequate for purposes of surgical division and repair.

A study of the secondary or lobar bronchi is next in order so that these observations may be applied to lobectomy performed by the principle of individual handling of the hilar structures. As far as the bronchi are concerned it is obvious that both upper lobes and the right middle lobe afford structures of sufficient length to allow amputation with subsequent closure of the stump. The lower lobes however present a somewhat different problem especially on the right side. Fig 1 A and B, shows

FIG 2 A

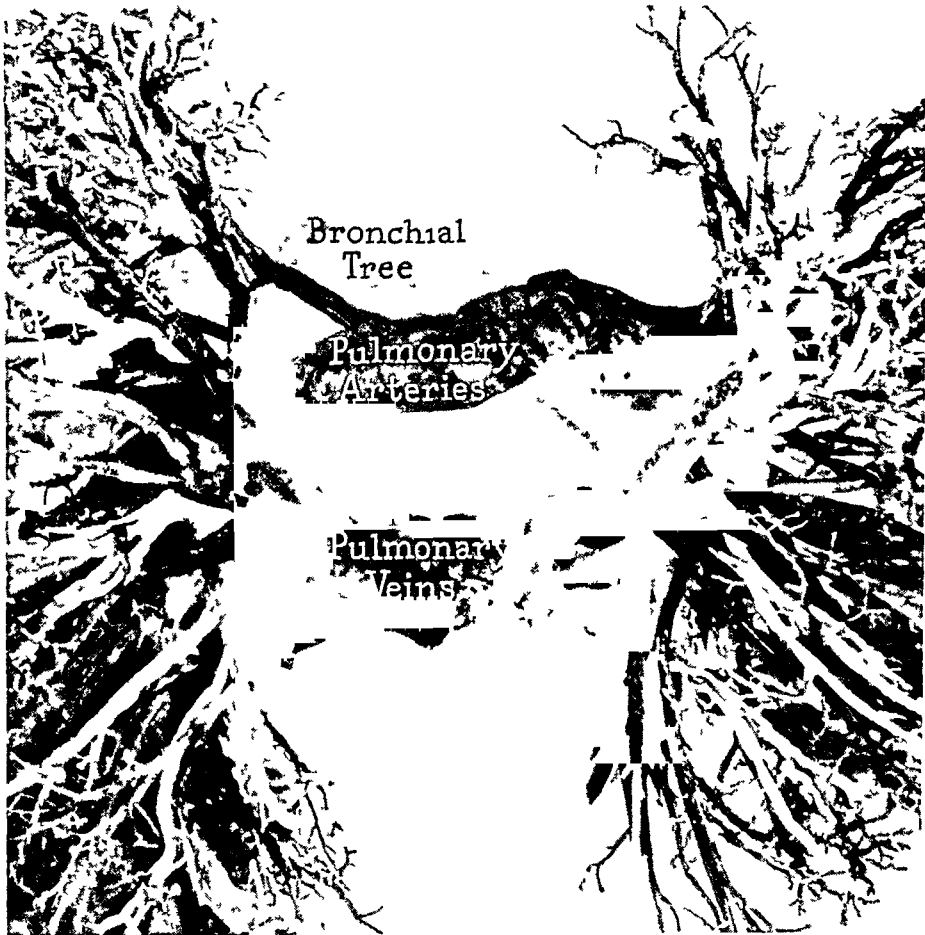


FIG 2 A—Injection mass cast of tracheobronchial tree, pulmonary arteries and pulmonary veins (anteroposterior view)

the relationships of the lower lobe bronchi and it is important to study the secondary bronchi which lead to the apices or superior divisions of the lower lobes. These bronchi are highly important for they represent the primary subdivisions of the lower lobe bronchi and also because it is sometimes possible, as pointed out by Churchill and Belsey,⁶ to resect either the superior division of the lower lobe alone or to remove the remainder of the lower lobe while leaving the superior division of the lower lobe intact. In performing complete lower lobe resection, the main bronchus to the lower lobe must be transected above the point of origin of this branch bronchus to the apex of the lobe. This is of particular importance on the right side because the

branch bronchus usually arises at about the level of the middle lobe bronchus the former springing from the posterior and the latter from the anterior aspect of the main bronchial axis. If the right lower lobe is to be resected the middle lobe bronchus must be preserved and must not be obstructed as a result of the removal of the lower lobe. It may, therefore be necessary to divide the bronchus to the apex of the lower lobe separately before the main trunk of the lower lobe bronchus at a point distal to the apical branch bronchus is exposed.

The surgical importance of the apices of the lower lobes cannot be overestimated. They have been aptly termed "a lobe within a lobe" because of the anatomic independence of the structures. Indeed, during an extensive study of many heart-lung specimens made at autopsy, the single outstanding anomaly has been one instance of three discrete lobes on the left.

FIG. - B



FIG. - B—Same from postero anterior view

The preparation of several injection-mass specimens has aided in the establishment of the relationships of the pulmonary arteries and veins to each other and to the bronchial tree. The lumens of these structures were filled with a synthetic resin of varied colors the tissues then being subjected to digestion by acids. Figure 2 A and B show the result of one such attempt. The principal information to be gained is orientation of the components

to each other. It can be seen that the pulmonary veins are anterior and inferior to the pulmonary arteries, which in turn are anterior to the right and left main bronchi. Study of the actual preparations yields a third dimension concept of the orientation of the important secondary and tertiary subdivisions of each major structure, but this cannot be demonstrated successfully in photographic illustrations. However, the pulmonary veins are well shown in Figure 2 and the relationships of the superior and the inferior pulmonary veins, the branches from the right middle lobe, the branches from the lingula, and the apical branches from the lower lobes to the inferior pulmonary veins are all clearly depicted.

FIG 3 A

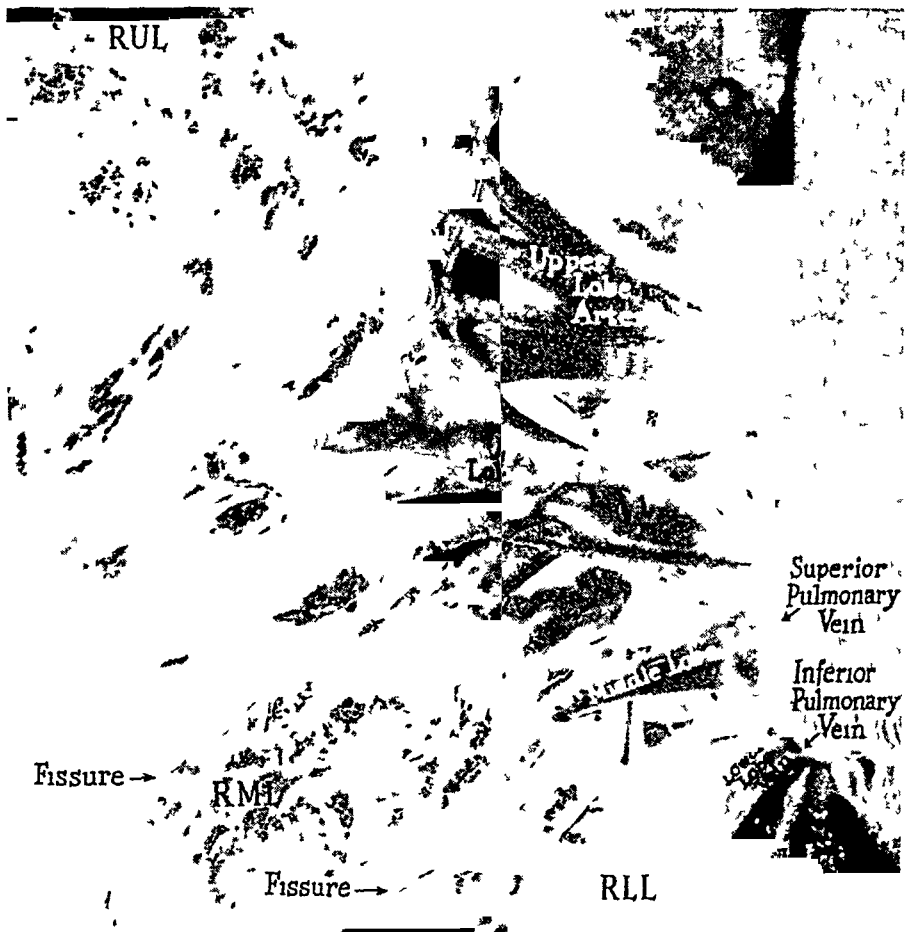


FIG 3 A—Dissection of right lung root, anterior aspect. The relationship of the pulmonary veins, the right pulmonary artery and the right main bronchus are emphasized.

Figure 3, A illustrates the structures of the right pulmonary hilum as viewed from the anterior aspect. The superior pulmonary vein with its tributary from the middle lobe is clearly demonstrated and the inferior pulmonary vein from the lower lobe can be seen without difficulty. It is our belief that pulmonary resection may be performed more safely if the veins are disposed of first because the avenue of entry for air or other embolic matter is thus closed. The veins lie on the anterior surface of the

PULMONARY RESECTION

hilum just beneath the pleural reflection which covers the lung root. The superior pulmonary vein is easily located, but it is sometimes more difficult to isolate the inferior pulmonary vein. The inferior vein, either right or left, lies upon the anterior surface of the respective inferior pulmonary ligament close to the hilar end of the ligament. Pursuit of the inferior pulmonary ligament, therefore has been found to offer an excellent approach to the inferior pulmonary vein. Figure 3, A also reveals the relationship of the arterial branch to the right upper lobe, to the veins, and to the right main bronchus

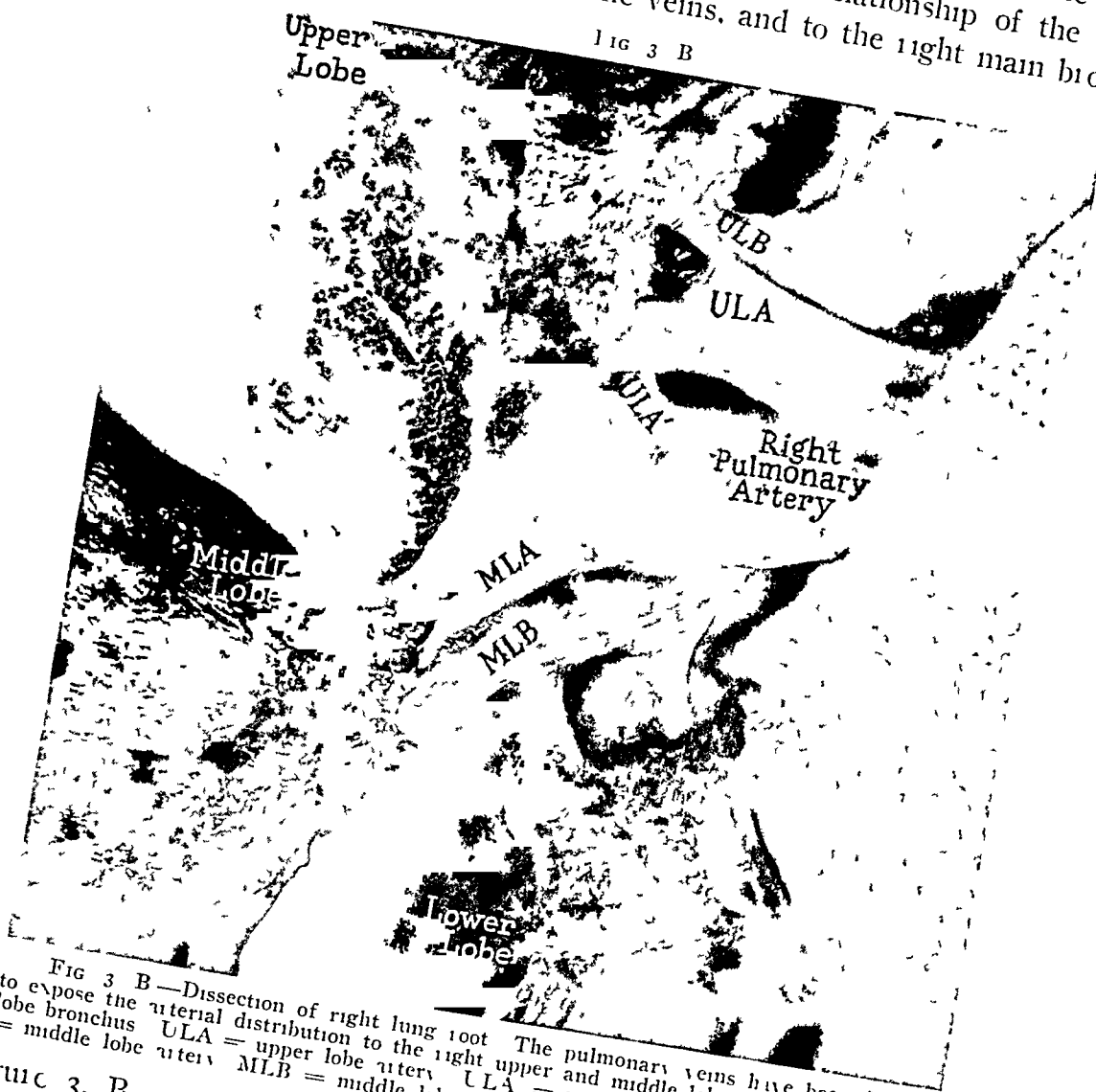


FIG 3 B—Dissection of right lung root. The pulmonary veins have been divided to expose the arterial distribution to the right upper and middle lobes. (ULB = upper lobe bronchus, ULA = upper lobe artery, MLA = middle lobe artery, MLB = middle lobe bronchus)

Figure 3, B represents an illustration made after the pulmonary veins have been divided and allowed to retract. From this aspect it is possible to see the arterial distribution to the right upper and middle lobes and the main trunk of the right pulmonary artery. It can be seen that in addition to the main arterial branch to the upper lobe there are accessory branches which arise independently. The main arterial branches to the upper and middle lobes closely parallel the bronchi to the respective pulmonary segments. It is clear that both the arterial branches and the bronchi to these two lobes are adequate for individual dissection, division and closure

FIG 4 A



FIG 4 A—Dissection showing vascular supply to right lower lobe

FIG 4 B



FIG 4 B—The vein has been removed so that arterial relationships may be emphasized (ULA = accessory upper lobe artery MLA = middle lobe artery MLA = accessory middle lobe artery)

PULMONARY RESECTION

Figure 4. A affords a view of the arterial and venous distribution to the right lower lobe as seen from the lateral aspect with the upper and middle lobes retracted to allow exposure. Here again, the venous tributary from the closely parallel the bronchus. However, since the venous channels from the anterior aspect, Figure 4. B is presented to demonstrate the arterial distribu-

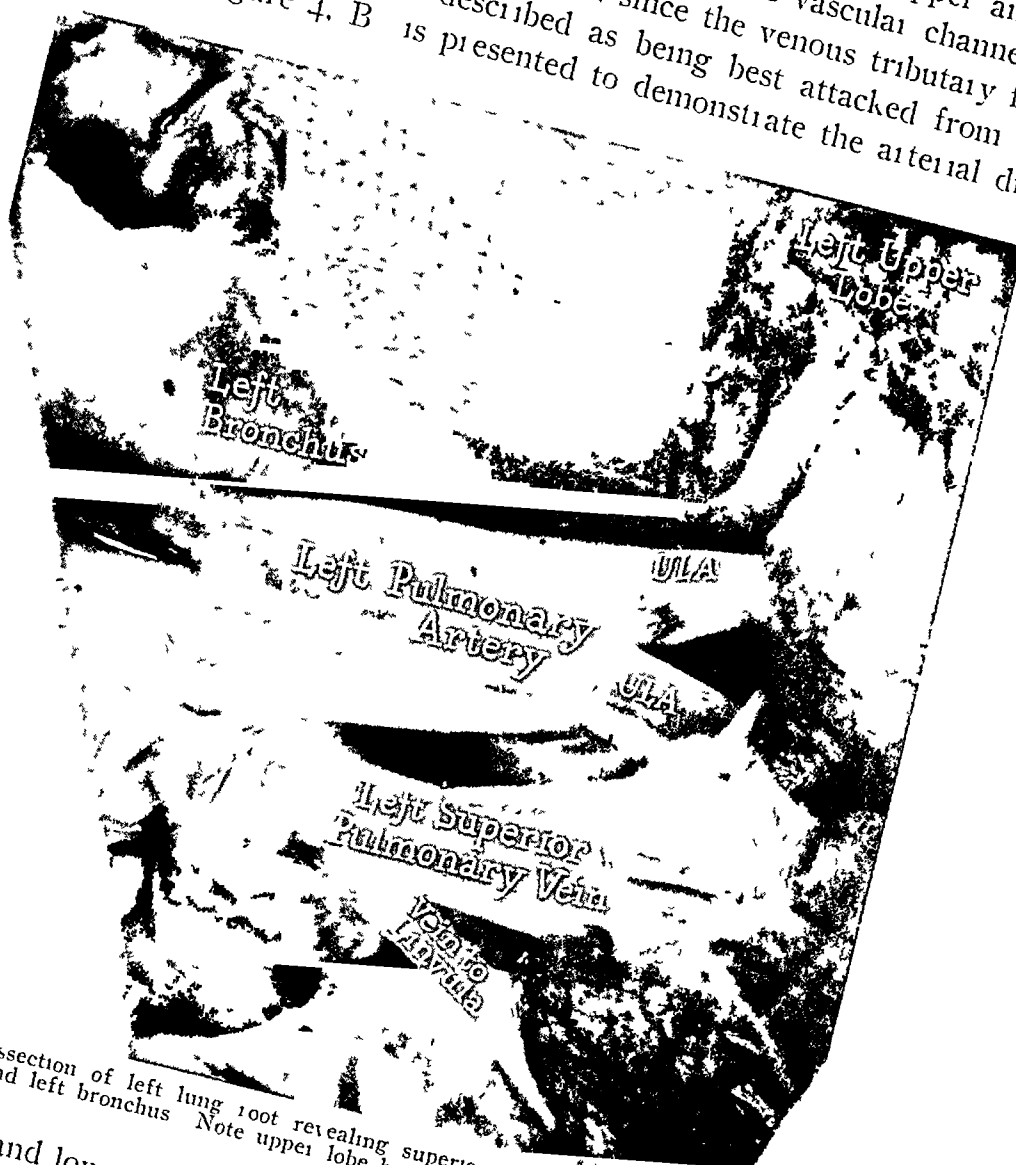


FIG 5—Dissection of left lung root revealing superior pulmonary vein, left pulmonary artery and left bronchus. Note upper lobe branches of pulmonary artery (ULA)

tion to the middle and lower lobes with their relationships. In this specimen there were two arterial branches to the middle lobe, each closely paralleling the bronchus. The arterial trunk continues onward to the lower lobe but as in the case of the bronchus, the large primary subdivision is that to the apex of the lower lobe. Again as in the case of the bronchus this arterial subdivision arises at approximately the same level as do the middle lobe branches. The implications of this observation are quite clear and they are to be applied to the anatomic approach to the right lower lobe resection. On the left side, the pulmonary veins are much like those described for the right side. Just as the middle lobe vein empties into the right superior pulmonary vein so does the vein from the lingula empty into the left superior pulmonary vein. In repetition let it be stated that the left inferior pulmonary

vein may be approached with certainty by pursuing the anterior surface of the left inferior pulmonary ligament.

The left pulmonary artery requires special consideration since in our opinion, this vessel and its branches do not lend themselves to individual dissection and ligation for lobectomy as well as do the counterparts on the right side. First the left pulmonary artery passes across the anterior aspect of the left main bronchus. Thereafter it differs from the right pulmonary artery in that it ascends over the left main bronchus to enter the fissure between the upper and lower lobes. Figure 5 demonstrates this orientation of the vessel as seen from the anterior aspect. Also it can be

FIG 6 A

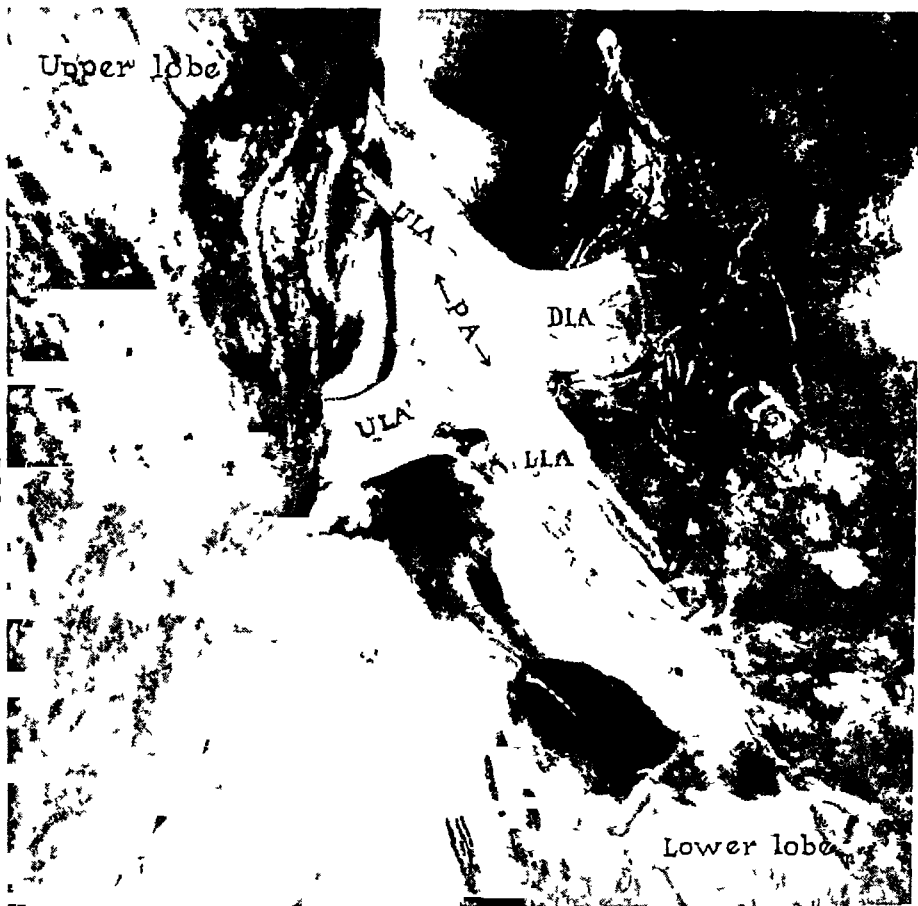


FIG 6 A—Dissection in the depths of the left great fissure which revealed the arterial pattern most commonly found on the left side. The main trunk of the left pulmonary artery is shown (PA) as it courses downward and forward deep in the interlobar fissure. There are two additional branches to the upper lobe (ULA and ULA') and there are two branches to the lower lobe, the superior division or apical branch (DLA) and the terminal division of the artery (LLA). There is gross similarity to the pattern seen on the right side, the arterial division to the lingula (ULA') corresponds closely to the middle lobe artery seen on the right side. While it may be preferable to ligate the lower lobe arterial divisions separately, the main trunk may be ligated safely because there is always adequate blood supply to the upper lobe from numerous branches originating at a higher level.

seen that the artery immediately gives off branches to the upper lobe which become numerous and are short. Figure 6, A, is a view of the left pulmonary artery as it continues onward into the fissure between the upper and lower lobes. Here additional short branches to the upper

lobe can be seen. The artery terminates in the lower lobe, but a major branch can be seen which supplies the apex of the lower lobe. Just as in the case of the relationships of the arteries to the right middle lobe and the apex of the right lower lobe, the branch to the lingula arises at about the same level as that to the apex of the left lower lobe. It should be pointed out, however, that the lingula is the recipient of a very rich blood supply from adjacent areas of the left upper lobe and thus it would not suffer from the loss of the branch shown in the illustration. Figure 6, B.

FIG 6 B



FIG 6 B—A similar dissection of another specimen. Here the pattern is complicated by more numerous arterial branches to both the left upper and lower lobes. (ULA' = accessory arterial branches to left upper lobe. LLA = terminal trunk to lower lobe. LLA' = accessory vessel to lower lobe)

illustrates a similar view of a dissection of another specimen. Here the arterial pattern is even more complicated than in Figure 6, A. There are more branches to both the upper and the lower lobes and these observations are of great important in partial lobectomy by the anatomic approach. They do not militate against successful application of the principle of individual dissection, division and closure of the structures when the left lower lobe is to be removed because, as has been pointed out, the sacrifice of one or more of the arterial branches to the upper lobe cannot be expected to compromise the pulmonary arterial circulation in the remaining left

upper lobe We are not at all certain however, that the anatomic approach can be applied with success to resection of the left upper lobe There are numerous branches from the main left pulmonary artery which are short and which may be difficult to expose It is conceivable that resection of the left upper lobe by any technic might result in obstruction of the main trunk thereby compromising the pulmonary circulation in the remaining lower lobe Since the pulmonary artery lies in the fissure between the upper and lower lobes, it is possible, for example, that a mass ligature about the stump of the left upper lobe would include some part of the artery thus obstructing the vessel

The bronchial arteries provide the systemic circulatory pathways to the lungs Observations have led to the conclusion that the position of these vessels is subject to great variation Furthermore they are rather small and it is to be questioned that they play any real part in maintaining viability of the lungs In any case these vessels have not contributed a problem during the performance of pulmonary resection The bronchial arteries are easily dealt with when encountered Indeed we have been impressed by the fact that these vessels are not seen at all in many instances

The state of the fissures between the lobes of the lungs is an important consideration While a truly complete fissure rarely exists in man it is often possible to extend an incomplete fissure to a point which at least approaches the required state A study of facts about fissures has yielded the information that the middle and upper lobes are very rarely separated by a cleft of any completeness Furthermore, the apical portions of the lower lobes are usually contiguous with adjacent areas of the upper lobes Once the incomplete fissure has been developed between clamps the satisfactory suturing of the divided surface of the lung has been something of a problem To date, the use of the running lock-stitch has yielded the greatest satisfaction because it gives positive control of bleeding from the cut surface and when tied tightly it does not draw through to pucker the sutured portion of tissue

The approach to the veins, arteries and bronchi is an important phase of pulmonary resection by this method The attack upon the veins can be made through the pleural reflection which covers the anterior surface of the pulmonary hilum An approach to the inferior pulmonary vein using the inferior pulmonary ligament as a guide has been described The veins from the middle lobe and from the lingula empty into the right and the left superior pulmonary veins However we have seen some instances in which the vein from the middle lobe has existed as an independent third right pulmonary vein

The approach to the main pulmonary arteries can be made in several ways Perhaps the simplest one is made from the anterior aspect after the veins have been divided These great vessels are in reasonably close association with their corresponding main bronchi and can usually be found without great difficulty The chief arterial trunk to the right upper lobe can be exposed best from the anterior aspect much as is the main trunk of

the right pulmonary artery. It is important that both the main trunk and its branch to the upper lobe be identified when the latter is to be ligated.

The arterial branches to the left upper lobe are numerous and can be found all the way from the superior aspect of the lobe root to a point well down into the interlobar fissure. The lowest branch or branches to the upper lobe are those supplying the lingular division of the lobe. The arteries to the left lower lobe are found in the depths of the interlobar fissure. In some instances these vessels stand out prominently, while in others they are completely obscured by the fusion of adjacent lung tissues of the two lobes.

The arteries supplying the right middle and lower lobes are best approached through the fissure between the upper and lower lobes. The branches to the middle lobe and to the superior division of the lower lobe commonly arise at about the same level and this point must be taken into consideration.

Once the arteries and veins have been dealt with, there is little left save the bronchus. The care with which a repair is made will appreciably influence the results in any series of cases. We are not satisfied that the best method of accomplishing this closure has been found, but its importance is so great that improved technics are constantly being sought, both by experimental means and clinical application. The pulmonary veins empty directly into the right auricle of the heart and, when very short, may require ligation of the individual tributaries rather than the main trunk. It is to be borne in mind that these structures pass through the pericardial space and that it is quite possible to open the pericardium unless care is exercised when the veins are exposed.

Preference for the individual ligation technic is based upon improved clinical results. The incidence of postoperative pleural infection is reduced, the character of the infection is more benign when it does occur. The incidence of postoperative bronchial fistula is definitely decreased, and the postoperative morbidity and mortality are favorably influenced.¹ These results are largely the consequences of a greatly improved closure of the bronchus and the elimination of a mass of strangulated, infected tissue at the stump. It is conceivable that application of individual dissection and management of the structures of the lobe root, combined with the use of chemicals of the sulfonamide group in the pleural cavity at operation, will one day make it possible to perform partial pulmonary resection with a low incidence of postoperative pleural infections.

REFERENCES

- ¹ Rienhoff, W. F., Jr. Pneumonectomy. A Preliminary Report of the Operative Technique in Two Successful Cases. *Bull. Johns Hopkins Hospital*, **53**, 390, 1933.
- ² Clafoord, C. On the Technique of Pneumonectomy in Man. *Acta chir. Scandin.*, Stockholm, **81**, Suppl. 54, 1937.

- Mason, G A Extirpation of Lung, (Hunterian Lecture, abridged) Lancet, 1, 1047, 1936
- * Blades, B, and Kent E M Individual Ligation Technique for Lower Lobe Lobectomy Jour Thor Surg 10, 84, 1940
- * Kent, E M, and Blades, B The Surgical Anatomy of the Pulmonary Lobes Jour Thor Surg (In press)
- * Churchill, E D, and Belsey, R Segmental Pneumonectomy in Bronchiectasis ANNALS OF SURGERY, 109, 481, 1939
- * Churchill, E D Resection of the Lung Surgery, 8, 961, 1940

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ANNALS OF SURGERY
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BRIEF COMMUNICATIONS



MEDIASTINAL GOITER

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IN 1931, Cattell¹ classified lesions arising from aberrant thyroid tissue and mentioned one extremely rare intrathoracic form in which there was no connection between the tumor and the main body of the thyroid gland. The case herewith reported is an example of this group. It should not be confused with the common intrathoracic form of goiter which develops through enlargement of nodules from the lower poles of the thyroid lobes that have become entrapped in the superior straits of the thoracic cage so well described by Lahey.²

Several mediastinal tumors of thyroid origin have been reported during the past few years. Harrington³ removed a tumor from just beneath the aortic arch which was found to be adenocarcinoma of thyroid origin. Colloid goiter in mediastinal locations was reported by von Haeberle⁴ with successful removal following division of the sternum, while Roholm's⁵ case was diagnosed by aspiration biopsy and treated by roentgenotherapy. Eliason⁶ and Bradshaw⁷ have mentioned successful surgical extirpations of true mediastinal goiters.

Case Report—R. J. white, female, age 19, was admitted to the Surgical Service of the Presbyterian Hospital April 10, 1939. Her previous history was of importance, for in November 1935, she had been admitted to this same hospital at which time studies—not including roentgenographic visualization of the chest and neck—were made for thyroid enlargement. The essayist resected nontoxic nodular portions of each lower thyroid pole. A search revealed no nodules in the upper mediastinum or behind the trachea. The recovery was uneventful. Histologic report of the tissue was that of fetal adenoma. Several follow-up visits were made on one of which in 1936 a roentgenologic study of the chest and neck was made. To our discomfiture, a tumor the size of a hen's egg was discovered in the right posterior mediastinum opposite the body of the 2nd thoracic vertebra. Discussion of therapy with her parents availed nothing.

Her second admission to this hospital was caused by a severe bronchopneumonia, on February 8, 1939. She made a good recovery, without complications. Roentgenologic studies of the chest during this admission showed an increase in the size of the tumor. It was reported as a smooth rounded tumor in the right posterior mediastinum extending from the level of the bodies of the 2nd to 5th thoracic vertebrae (Fig. 1A and B).

After somewhat less than two months convalescence, she was readmitted to the hospital at the insistence of her family, who had been informed of the increase in size of the tumor, which, however, had caused no symptoms. Because of the patient's approaching marriage her parents not only listened to advice but readily acquiesced to surgical management of the lesion.

* Read before The Philadelphia Academy of Surgery, February 3, 1941.

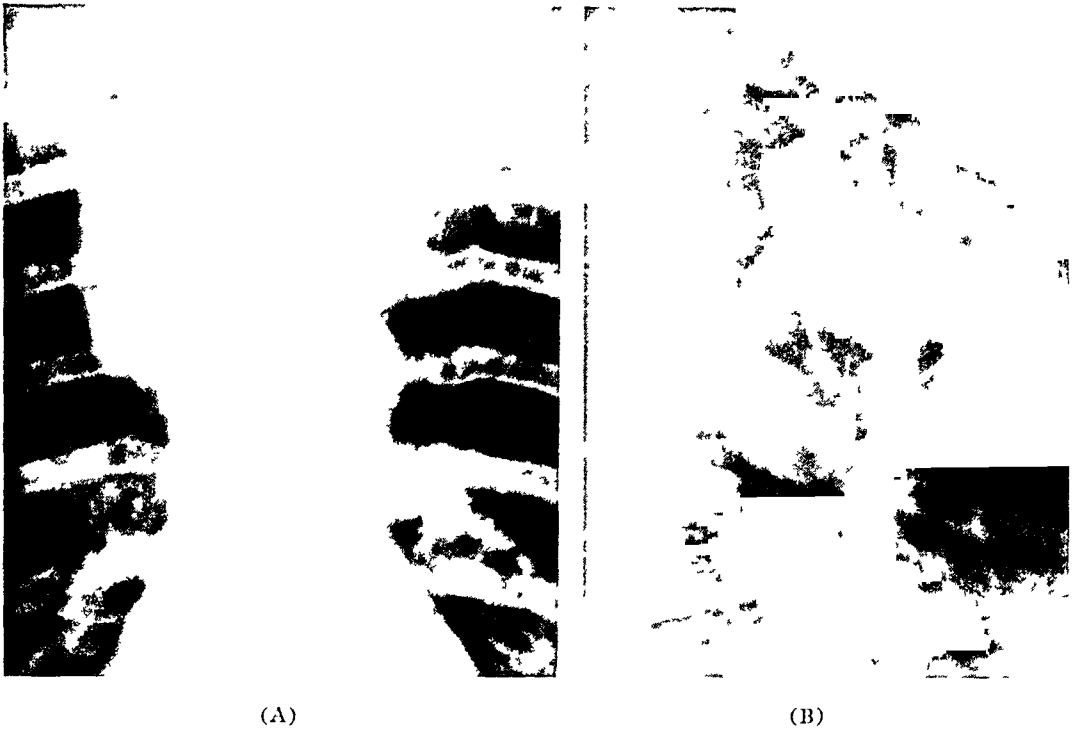


FIG 1—(A) Anteroposterior roentgenogram showing the extent of the tumor mass. (B) Lateral roentgenogram showing the tumor mass and its relation to the air-filled trachea and the esophagus containing barium mixture.

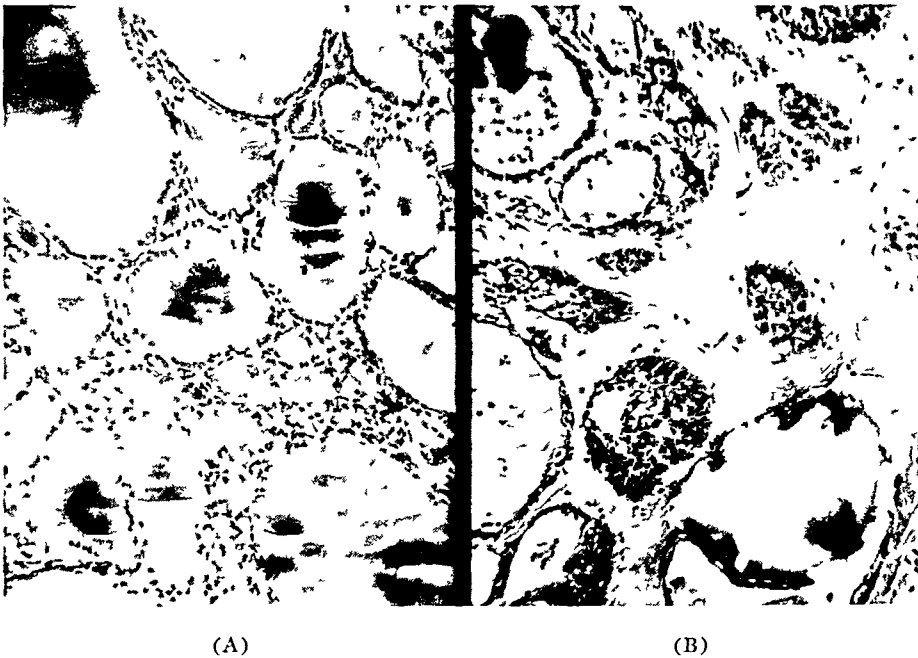


FIG 2—(A) Photomicrograph showing typical acinar formation of a nontoxic nodular goiter. (B) Photomicrograph showing acinar areas containing colloid, others containing sheets of epithelial cells and, also, an excessive amount of fibrous tissue between the acini.

Pertinent studies of blood chemistry, blood count, serology and urinalysis showed normal figures. The basal metabolic rate was within normal range. Vocal cords approximated normally. Barium visualization of the esophagus revealed no compression while roentgenograms of the chest confirmed earlier findings and location of the tumor. Physical examination revealed no chest signs, and a local palpation of the thyroid area showed freedom from recurrence in either lobe.

Operation—April 15, 1939. Under cyclopropane intratracheal anesthesia, the mediastinum was entered through a right posterior incision. A curving incision about one inch medial to the vertebral border of the scapula was made through skin, subcutaneous tissue and muscle down to the ribs. A section of the 5th rib was removed close to the spine and its bed was carefully excised, without piercing the pleura. The parietal pleura



FIG. 3—Follow up anteroposterior roentgenogram showing area previously occupied by the tumor.

was mobilized from this point upwards and downwards and the 6th, 4th and 3rd ribs were rapidly sectioned. Mobilization of the pleura was continued until the tumor was adequately exposed. It was smooth, rounded, and cystic in consistency, red-brown in color and between three and four inches in diameter. It rested against the right anterior aspect of the bodies of the thoracic vertebrae from the lower border of the 2nd thoracic to the upper border of the 6th thoracic. The lung hilus was anterior and below. Internal to the tumor were the trachea and esophagus. In this latter organ an esophagoscope had been placed as a guide. The great vessels and brachial plexus were above and anterior. There was no palpable connection with the thyroid gland in the neck nor with any structure in the mediastinum, other than the tumor-bed. The capsule of the tumor was incised and it was enucleated with ease. The capsule was closed by interrupted catgut suture which controlled bleeding. The tissue removed was cystic and nodular and of the

consistency of adenomatous thyroid tissue. A cigarette drain was brought down to the tumor bed through an opening in the old collar incision. This unusual placement was an error—though it was done to save the prospective bride a possible draining back-sinus. The rib ends were approximated with chromic catgut, and the incision closed in layers, without drainage. A transfusion of 500 cc of citrated blood was begun shortly before conclusion of the operation through a cannula which had been placed in a foot vein before beginning the operation.

Immediate convalescence was uneventful until the 5th day, at which time the catheter which had been placed through the cigarette drain to the tumor-bed ceased to respond to suction. On the 10th day (April 25) a septic temperature developed, and roentgenograms of the chest showed a fluid level, extrapleural in location. Culture of this fluid showed hemolytic *Staphylococcus aureus*, *Streptococcus viridans* and *Bacillus proteus*. Reestablishment of drainage caused abatement of the fever. Time was lost by improper use of chemotherapy (i.e., without proper drainage) so that a persistent, variable increase in temperature persisted. On the 43rd day the posterior incision was opened and thick yellow pus was evacuated, which showed the previously mentioned bacterial flora. The septic temperature ceased and the wound healed rapidly. Seventeen days later, roentgenograms of the chest showed almost complete disappearance of mediastinal and retropleural densities. The patient was discharged June 22, 1939.

Pathologic Report—Dr Philip Custer. Tumor mass seven centimeters in diameter, weighing 105 grams, multilocular, thin capsule filled with cystic areas each containing red-brown material. Microscopic examination revealed thyroid tissue in irregular acinus formations, except in one area where there was fibrous tissue, and in a few other areas solid sheets of epithelial tissue lined the cystic spaces. It is not possible to tell whether this is metaplasia, or that it is a mixed tumor made up almost exclusively of thyroid tissue (Fig 2A and B). *Pathologic Diagnosis*. Aberrant thyroid.

Follow-Up Visits. The patient made several follow-up visits. Roentgenograms of the chest, taken September 1, 1939, showed thickened pleura and malposition of the fragments of the third rib (Fig 3). This deformity was due to the poor selection of material to oppose the fragments. The patient was married September 15, 1939. Her last follow-up visit made in the spring of 1940. She had gained considerable weight and strength, and was well in all respects.

SUMMARY

The successful removal of a posterior mediastinal, nontoxic nodular goiter by extrapleural mediastinotomy and complicated by secondary extrapleural hemolytic *Staphylococcus aureus* and *Streptococcus viridans* infection is recorded.

Acknowledgement is made to Dr William Bates, Chief of Surgical Service in the Presbyterian Hospital, for his aid and advice in this case.

REFERENCES

- ¹ Cattell, R. B. Aberrant Thyroid. JAMA, **97**, 1671, 1931.
- ² Lahey, F. H. Intrathoracic Goiter. JAMA, **113**, 1098, 1939.
- ³ Harrington, S. W. Surgical Treatment of Mediastinal Tumors. ANNALS OF SURGERY, **96**, 843, 1932.
- ⁴ von Haberer, H. A Retrosternal Goiter Located in the Posterior Mediastinum. Zentralbl f chir, **65**, 906, 1938.
- ⁵ Roholm, K. A Retromediastinal Goiter Diagnosed by Aspiration Biopsy. Hospitalstid, **81**, 853, 1938.
- ⁶ Eliason, E. L. Personal communication.
- ⁷ Bradshaw, H. W. Personal communication.

BOOK REVIEW

THE SURGERY OF PANCREATIC TUMORS By Alexander Brunschwig, M D, St Louis, Mo C V Mosby Co 1942

IN THESE HECTIC DAYS of global warfare one must admire the courage and faith of the author, and of the publisher, of a monograph not related to any phase of our present emergency. But in reviewing the comprehensive and authoritative volume by Dr Alexander Brunschwig on the "Surgery of Pancreatic Tumors," we would emphasize the fact that the author has been studying the subject and contributing to it for many years. The motive and purpose of the monograph is best presented in Brunschwig's introduction. "A medical treatise may be written to cover a large and well known field and thus serve as a review, and for instructional progress, or it may deal with controversial subjects and thus afford its author the opportunity to state his own views, or it may deal with relatively few facts in a newly developing field and serve to stimulate further work in this field. It is in this latter spirit that this treatise was written. A summary of most of the recorded experiences in the surgery of all types of pancreatic tumors is attempted, with the hope that it might contribute in some small measure to the maintenance of interest in this branch of operative surgery, especially in regard to malignant growths."

The first chapter, reviewing the history of the experimental pathology and surgery of the pancreas and the early attempts to deal with malignancy of the organ, shows a thorough study of the literature. Especially interesting are the references to the early contributions of Brunner and of Graaf. This historical review is, in itself a unique contribution. Chapters II, III and IV take up in detail the anatomy and physiology and the experimental surgery, respectively, and add very materially to the value of the book as a monograph on the pancreas, aside from the main theme of neoplasms of that organ.

The chapter on diagnosis of pancreatic lesions and diagnostic procedures is followed by one on preoperative and postoperative care. Both of these are comprehensive, give all the newer advances, and do not repeat out-of-date and useless tests and methods.

Three chapters deal with pancreatic cysts, followed by one devoted to cystadenomata and cystadenocarcinomata. Lesions of the ampulla of Vater, with a discussion of differential diagnoses, are considered at length.

The next seven chapters discuss the most recent advances in the surgery of the pancreas, five of these on carcinoma of the acinar and duct epithelium, followed by two chapters on islet cell tumors. These are original comprehensive contributions to new fields of surgery and in themselves could be given the title of the monograph. These pages deal with new data in a newly developing surgery and serve to stimulate further work in this field. They constitute a summary of most of the recorded and much of the unpublished experiences in the surgery of all types of pancreatic tumors.

From this brief review, it is obvious that Dr Brunschwig's monograph is as much a treatise on the pancreas as on the tumors of the pancreas. But the reviewer would emphasize again the original contributions to the newer surgery of the tumors of the pancreas that Dr Brunschwig has made in this book.

ALLEN O WHIPPET M D

BOOKS RECEIVED

- THE BLOOD BANK AND THE TECHNIQUE AND THERAPEUTICS OF TRANSFUSIONS By Robert A Kilduffe and Michael DeBakey M D St Louis C V Mosby Co, 1942
- NEUROANATOMY By Fred A Mettler, M D St Louis C V Mosby Co, 1942
- THE 1941 YEAR BOOK OF PATHOLOGY AND IMMUNOLOGY Edited by Howard T Kaisner, M D, and Sanford B Hooker A M, M D Chicago The Year Book Publishers 1941
- SYNOPSIS OF GENITOURINARY DISEASES By Austin I Dodson, M D, F A C S St Louis C V Mosby Co 1941
- ROENTGEN TREATMENT OF INFECTIONS By James F Kelly, M D, F A C R, and D Arnold Dowell M D Chicago The Year Book Publishers Inc 1942
- SURGERY OF THE AMBULATORY PATIENT By L Kraeer Ferguson, M D With a Section on Fractures By Louis Kaplan M D Philadelphia J B Lippincott Co, 1942
- SYNOPSIS OF ANO-RECTAL DISEASES By Louis J Hirschman, M D, 2nd Ed St Louis C V Mosby Co 1942
- THE HISTORY AND EVOLUTION OF SURGICAL INSTRUMENTS By C S S Thompson, M D, New York Schuman's, 1942
- ANATOMY OF THE HAND By Frederic Wood Jones D Sc, F R S, F R C S, Professor of Anatomy, University of Manchester 2nd Ed Baltimore, Williams & Wilkins Co, 1942
- ACUTE INJURIES OF THE HEAD By G F Rowbotham B Sc, F R C S Baltimore Williams & Wilkins Co 1942
- THE BLOOD IN CANCER By O Cameron Gruner, M D Montreal Renouf Publishing Co, 1942
- BLOOD GROUPING TECHNIC By Fritz Schiff, M D and William C Boyd Ph D New York Interscience Publishers Inc, 1942
- THE SURGERY OF PANCREATIC TUMORS By Alexander Brunschwig, M D St Louis C V Mosby Co, 1942
- FRACTURES DISLOCATIONS AND SPRAINS By John Albert Key, M D and H Earle Conwell, M D St Louis C V Mosby Co 1942
- PHYSICIAN'S REFERENCE BOOK OF EMERGENCY MEDICAL SERVICE New York E R Squibb & Sons 1942
- THE CARE OF THE ACID (GIRIAIACS) By Maltoid W Thewlis M D St Louis C V Mosby Co, 1942
- CINIPLASTIC OPERATIONS By Rudolph Nissen, M D, and Ernest Beigmann M D New York Grune & Stratton 1942
- DIAGNOSTICO DE LOS TUMORES ABDOMINALES By Pablo L Muzzi M D Vol I 1941, and Vol II 1942 Libreria y Editorial, 'El Ateneo' Buenos Aires Argentina
- CHINA'S HIGH PRICES By Szeming Sze M A M B B Ch (Cantab) New York China Institute in America Inc 1942

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CARCINOMA OF THE BREAST*

I—RESULTS OF TREATMENT

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AMONG most of those who deal with carcinoma of the breast today, there has been a sobering realization that the high hopes of the curative value of radiation that were held a decade or more ago have not been fulfilled. We face the fact that we must turn back to surgical removal of the disease, try to choose our cases for radical mastectomy with more exactitude, and perform the operation with more skill. In this task many factors of clinical and pathological judgment play a part, and our primary need is for more and better data upon which to base our decisions. It is with this end in view that we present the data regarding the treatment of carcinoma of the female breast at the Presbyterian Hospital in New York over a 20-year period, from 1915 to 1934, inclusive.

These data have several advantages. The number of cases is fairly large, totaling 1040. The unit records of these cases have been kept with comparative completeness. Most of them include clinical photographs. Dr. Hugh Auchincloss, who has had a special interest in this group of cases, made careful descriptions of the clinical findings, and sketches in many cases. The histologic study of the tissues removed has been carried out with thoroughness. Finally, the follow-up has been fairly complete.

The Method of Analysis. In studying this material we have utilized a method which we believe is specially advantageous when a detailed analysis of a large number of cases has to be made, namely, the punch-card method. We have been fortunate in having the advice and assistance of Miss Dorothy Kuitz, Supervisor of the Presbyterian Hospital Record Room, an authority on the use of the punch-card method in medical problems.

A special summary sheet listing some 700 different items to which reference might be made was first drawn up, and mimeographed. The data from the individual case histories were then carefully transferred to these summary sheets. Where contradictory clinical findings were found recorded, as sometimes happened, they were studied critically and the truth determined as well as possible by checking the descriptions against

* Aided by the Leggett and Watters Fund for Cancer Research

the photographs, *etc* Cards were finally punched from the summary sheets, and these cards sorted in the tabulating machine to determine the correlations in which we were interested

In this way it is not only possible to work out the correlations between any number of different factors with ease, but the findings can be checked and counterchecked in a way that is scarcely possible by hand sorting and arithmetic Our experience with the punch-card method leads us to recommend it strongly to all who wish to analyze extensive and complex medical data

In this first communication we propose to present the basic facts about carcinoma of the female breast which the study has revealed They are recorded for what they are worth, without comparison with the findings of others, because the variables influencing statistics as they have been computed in the past are so numerous and so dependent upon human emotions that in regard to this subject comparisons are indeed odious The few comments which we have made express our own opinions, and not necessarily those of the other members of the staff of our institution In future studies we shall discuss certain phases of the subject in greater detail, such as the criteria governing our choice of treatment, the relationship of histopathology to prognosis, *etc*

The Data—The records of all women with proved or presumed carcinoma of the breast coming to the Presbyterian Hospital between the years 1915 and 1934, inclusive, were included (Table I)

TABLE I
CARCINOMA OF THE FEMALE MAMMARY GLAND
Presbyterian Hospital (1915 to 1934 inclusive)

Total number of patients applying for treatment	1040
I—Patients examined in Out-Patient Department and turned away	
detailed unit records not made	54
II—Patients accepted for study and detailed unit records made	986
A—Previously treated elsewhere	110
B—Primary cases	873
1—Private cases	253
2—Ward cases	626

Presenting Symptoms—There are some features of interest regarding the symptomatology which led these patients to seek medical aid Table II lists the presenting symptoms in the ward cases Private cases have not been included because their histories were often less complete than those of ward patients

The fact that in 66 per cent of these patients an unsuspected carcinoma was discovered in the course of a routine physical examination, made when the patient came for symptoms elsewhere than in the breast, is striking proof of the value of careful and complete physical examination of every patient

The infrequency of pain as the presenting symptom of breast carcinoma is well known Only 16 per cent of our patients sought medical aid because of pain

CARCINOMA OF THE BREAST

TABLE II

PRESENTING SYMPTOMS IN PRIMARY WARD CASES

Total number primary ward cases	623
Manner of diagnosis not stated	14 or 2.2%
Came to hospital complaining of symptoms elsewhere than in breast Breast carcinoma discovered during routine physical examination	41 or 6.6%
Came to hospital complaining of symptoms in breast	568 or 91.2%
Complained of tumor in breast	536
Complained of other breast symptoms	32
Erosion of nipple	13
Pain in breast	9
Retraction of nipple	8
Enlargement of breast	8
Discharge from nipple	6
Itching or burning of nipple	4
Redness of skin over breast	3
Generalized hardness of breast	2
Shrinkage of breast	1

Disposition of Cases—The disposition of the 986 cases studied by us is shown in Table III

TABLE III

DISPOSITION OF CASES

I—Patients previously treated elsewhere	110
A—No further treatment by surgery or radiation	60
B—Further treatment by radiation	35
C—Further treatment by surgery	15
1—Palliative limited operation	3
2—Radical mastectomy	12
II—Primary cases	876
A—Not treated by surgery or radiation	119
B—Treated by radiation only	71
C—Treated principally or exclusively by surgery	686
1—Palliative limited operation	46
2—Radical mastectomy	640

It is upon this group of primary cases that we will focus our attention. The patients who had received treatment elsewhere before coming to the Presbyterian Hospital do not merit further discussion, for, in most instances, we have no exact description of the kind of treatment they had. Moreover, the number in which it seemed wise to do anything further was so small that the end-results in the group have no statistical significance.

Operability—It is customary to refer to the proportion of cases in which radical mastectomy is performed as the operability rate. This may be calculated in either of two ways, as follows: (1) *Relative* operability (the number of cases in which radical operation was done divided by the number of primary cases accepted in the clinic, or 640 divided by 876) 73.1% (2) *Absolute* operability (the number of cases in which radical operation was done divided by the total number of cases of all types seen in the clinic, or 640 divided by 1040) 61.5%

The latter figure is distorted to some extent by the fact that it contains a number of the patients who shop around from one hospital to another when their disease recurs and becomes incurable. Yet, it has the advantage of including all of the hopelessly advanced cases who are turned away without a detailed examination, and for this reason more closely approximates the

true limitations of surgery in the disease Expressed on this so-called absolute basis our operability rate is seen to be low

There was a total of 236 primary cases in our series in which radical operation was not done The reasons for this are detailed in Table IV

TABLE IV

CLASSIFICATION OF PRIMARY CASES *Not* TREATED BY RADICAL MASTECTOMY

I—Constitutionally inoperable (13 of these also inoperable because of extent of carcinoma)	28
II—Inoperable because of extent of carcinoma	133
III—Refused radical mastectomy	59
IV—Died of intercurrent disease before radical operation could be carried out	1
V—Referred elsewhere because of lack of accommodations	3
VI—Failed to return to Clinic	2
VII—Carcinoma mistaken for a benign lesion and radical mastectomy not done	10
Total	236

The question of the criteria of operability for breast carcinoma is such a complex one that we shall not discuss it further here, but will make it the subject of a separate paper

Follow-Up—The course of the disease in these patients was followed in the Out-Patient Department by the various attending surgeons who were responsible for their care A carefully planned follow-up system has long been a feature of the organization of the Department of Surgery of the Presbyterian Hospital, and all patients with malignant tumors who are accepted for treatment are followed for the remainder of their lives With ward patients this system has proved very satisfactory—417 of the total 422 ward patients with primary breast carcinoma treated by radical mastectomy were followed until they died, or for a minimal period of five years after operation This follow-up percentage of 98.8 per cent is, we believe, a good record for work done in a large city such as New York, where the poor change their residence frequently

With private patients the initiative for the follow-up is left to the attending surgeon, and it is an unfortunate fact that they have not done very well in the matter Only 182, or 83.5 per cent, of the total of 218 private patients with primary breast carcinoma treated by radical mastectomy were followed until death or for a minimal period of five years It should be stated that most of these failures in the follow-up occurred some years ago, in the practice of surgeons now retired from the hospital staff

Of the whole group of 640 primary cases treated by radical mastectomy, including both private and ward patients, 599, or 93.6 per cent, were followed until death, or for the minimal five-year period

Results of Radical Mastectomy—We have tried to make our presentation of the results of radical mastectomy in this series of cases as complete as possible Throughout all of the tables in which the correlations of results with a variety of different factors are considered, we have presented the local recurrence rate in the field of operation as well as the clinical cure rate Both of these computations have been made on the basis of five-year

results When local recurrence, metastasis, or death occurred later than five years after operation, as has been the case in a small percentage of patients, we have, nevertheless, counted these cases as five-year clinical cures We have also presented the five-year survival rate following radical mastectomy This group includes not only the patients who are still well but those who survive with known carcinoma at the end of five years

We have chosen the term "*five-year clinical cure*" to designate the group of patients who did not develop any further evidence of cancer during the five-year period following treatment, because it describes this group more accurately than any other word or phrase The phrase "five-year cure rate" has become common parlance among those who present cancer statistics, because it is shorter and grammatically more adaptable than the phrase "percentage of patients well at the end of five years" None of these phrases imply, of course, that permanent cures have been obtained We have added the adjective "clinical" to the phrase "five-year cure" merely to indicate our awareness of this fact

Table V shows the results in the total series of ward and private cases treated by radical mastectomy

TABLE V

FIVE-YEAR RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES

I—Number of radical mastectomies	640
II—Operative deaths	20 or 3.1%
III—Lost track of before 5 years	41 or 6.4%
IV—Died of unknown cause before 5 years	13 or 2.0%
V—Died of intercurrent disease before 5 years, without evidence of recurrence of carcinoma	12 or 1.9%
VI—Died of breast carcinoma before 5 years	290 or 45.3%
VII—Alive, with recurrence 5 years after operation	33 or 5.2%
VIII—Alive without recurrence 5 years after operation	231 or 36.1%

THESE RESULTS MAY BE EXPRESSED IN TERMS OF RELATIVE AND ABSOLUTE CURE AND SURVIVAL RATES AS FOLLOWS

Relative 5-year clinical cure rate (5-year clinical cures — number radical mastectomies or 231 — 640) =	36.1%
Absolute 5-year clinical cure rate (5-year clinical cures — total number patients seen or 231 — 1040) =	22.2%
Relative 5-year survival rate (5-year survivals — number radical mastectomies or 264 — 640) =	41.3%
Absolute 5-year survival rate (5-year survivals — total number patients seen or 264 — 1040) =	25.3%

The frequency and distribution of local recurrence and metastasis in the primary cases treated by radical mastectomy is shown in Table VI

We know that if our information were complete regarding the clinical findings at death in all of the patients who succumbed, the frequency of both local recurrence and metastases would be found to be higher than our figures indicate An effort was, indeed, made to follow all of our patients to the end, but in a considerable number this was impossible either because death occurred in a distant place, or because the patient was bedridden at home for a long time before she died, or because death took place in a nursing home or hospital that could not provide us with complete clinical data

Surgeons will do well to bear in mind the fact that the incidence of local recurrence in the field of operation continues to be distressingly high At the end of five years after operation it was 22.8 per cent in this series The

TABLE VI

FREQUENCY AND DISTRIBUTION OF LOCAL RECURRENCES AND METASTASES
WITHIN FIVE YEARS FOLLOWING RADICAL MASTECTOMY IN PRIMARY CASES

I—Total number of radical mastectomies	640
II—Number known to develop local recurrence within 5 years after operation	146 or 22.8%
A—In the operative field on the chest wall	130 or 20.3%
B—In the homolateral axilla	42 or 6.6%
III—Number known to develop metastases within 5 years after operation	316 or 49.4%
A—In lung or pleura	138 or 21.6%
B—In bone	114 or 17.8%
C—In supraclavicular regions	89 or 13.9%
D—In liver or peritoneum	63 or 9.8%
E—In opposite breast	58 or 9.1%
F—In contralateral axilla	49 or 7.7%
G—In regional skin or as <i>en cuirasse</i>	31 or 4.8%
H—Distant skin metastases	21 or 3.3%
I—In other sites	39 or 6.1%

obvious conclusion is that cases must be selected more carefully and the operation must be performed more thoroughly

Types of Radical Mastectomy—The 640 radical mastectomies in this series were performed by, or under the direction of, 36 different attending surgeons. This fact makes it difficult to classify the different types of operations that were undertaken, particularly since there was no general agreement among this group as to which type of operation is best. We have, nevertheless, divided the operations that were done into five groups, as follows

I—*Mastectomy and Axillary Dissection*—The breast was removed first, not including the pectoral muscles. A limited axillary dissection was then done. This type of procedure was done only a few times, and usually in those cases where the patient's general condition was poor.

II—*Limited Radical Mastectomy*—The breast, pectoralis major, and axillary contents were removed in one piece, but the pectoralis minor was not removed.

III—*Radical Mastectomy—Breast and Axillary Contents Removed Separately*—In this operation the breast and pectoral muscles were removed first, and then the axillary contents dissected out separately. This was the method preferred by the late Dr. George E. Brewer, and one or two surgeons have continued to use it in the Presbyterian Hospital.

IV—*Radical Mastectomy—Skin Flaps Approximated Without Grafting*—This is the usual type of radical operation, both pectoral muscles being included and the tissues removed in one piece. The amount of skin removed was limited, however, by the necessity of bringing the flaps together.

V—*Radical Mastectomy—Wound Grafted*—This was a more radical procedure, particularly as regards the removal of skin and subcutaneous tissue on the chest wall. Either pinch or Thiersch grafts were used to cover the defect.

Unfortunately this series fails to provide any significant information regarding the superiority of the classical Halsted technic for radical mastectomy. Only one of the ten operators who performed more than 25 of the operations in this series carried out the classical Halsted procedure, with wide removal

CARCINOMA OF THE BREAST

of skin and subcutaneous tissue and immediate Thiersch grafting of the defect This operator had a total of only 32 cases and his results are, therefore without statistical significance

The results in the five different types of operations that we have described are shown in Table VII

TABLE VII
RESULTS OF DIFFERENT TYPES OF RADICAL MASTECTOMY IN PRIMARY CASES

Type of Operation	No of Cases	Operative Deaths		5-Year Local Recurrence		5-Year Clinical Cures	
		No	Per Cent	No	Per Cent	No	Per Cent
I Mastectomy and axillary dissect	11	0	—	7	63 6%	2	18 2%
II Limited radical—pect minor not removed	8	0	—	2	25 0%	3	37 5%
III Radical—breast and axillary contents removed separately	53	1	1 9%	12	32 6%	21	39 6%
IV Radical—skin flaps approximated without grafting	401	14	3 5%	88	21 9%	140	34 9%
V Radical—wound grafted	167	5	3 0%	37	22 2%	65	38 9%
Totals	640	20	or 3 1%	146	or 22 8%	231	or 36 1%

There is surprisingly little difference in the local recurrence and clinical cure rates for the two different types of operation represented by enough cases to be of some significance, that is Types IV and V We would warn the reader, however, against drawing any conclusions regarding operative methods from this evidence for we believe that the technics of the many different surgeons who performed these operations varied so widely, even within the limits of the classification that we have made, that the evidence is of but little value

A different kind of evidence regarding operative technic, and a kind which probably does have some real value is that which concerns the length of time required for the operation This is shown in Table VIII

TABLE VIII
RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES ACCORDING TO LENGTH OF OPERATIONS

Length of Operation in Minutes	No of Cases	Operative Deaths		5-Year Local Recurrence		5-Year Clinical Cures	
		No	Per Cent	No	Per Cent	No	Per Cent
I 1 to 59 mins	56	1	1 8%	13	23 2%	16	28 6%
II 60 to 119 mins	255	7	2 7%	51	20 0%	90	35 3%
III 120 to 179 mins	239	11	4 6%	58	24 3%	82	34 3%
IV 180 to 239 mins	71	0	—	21	29 6%	31	43 7%
V 240 or more mins	16	1	6 3%	2	12 5%	9	56 3%
Time not stated	3	0	—	1	—	3	—
Totals	640	20	or 3 1%	146	or 22 8%	231	or 36 1%

We must point out that the number of cases included in Group V, in which the operation lasted 240 minutes, or more, is so small that the differences in local recurrence and clinical cure rates between this group and other groups are not statistically significant The difference in clinical cure rates between Group III and Group IV, however, is possibly indicative of true improvement in operative technic

The operative mortality in these data, shows a slight increase as the duration of the procedure is prolonged beyond two hours This again, however, is a factor which depends more upon the technic of the individual

operator than upon the actual length of the operation. The operative mortality of 3.1 per cent which occurred in this series of cases as a whole, between 1915 and 1934, is certainly somewhat higher than we need anticipate with present-day surgical technic. If proper care is taken to avoid operative shock by gentle handling of the tissues, the use of sharp dissection rather than scraping, tearing, and ripping apart of the tissues, and avoidance of dehydration of the tissues by keeping them covered with moist towels and compresses, we know that four or five hours can be devoted to the performance of this operation without raising the operative mortality above one per cent. It is our personal belief that this length of time is, indeed, needed to carry out the extensive and meticulous dissection required in the Halsted type of radical mastectomy.

As evidence that the surgical staff of the Presbyterian Hospital, as a whole, is coming around to the point of view that the more meticulous type of radical mastectomy is worth doing, Table IX, showing the length of radical mastectomy according to five-year periods, is presented.

TABLE IX
LENGTH OF RADICAL MASTECTOMY IN PRIMARY CASES ACCORDING TO FIVE YEAR PERIODS

Length of Operation	No. of Cases 1915 - 1919	No. of Cases 1920 - 1924	No. of Cases 1925 - 1929	No. of Cases 1930 - 1934s
0 - 59 mins	28	15	11	2
60 - 119 mins	65	52	81	57
120 - 179 mins	32	58	60	89
180 - 239 mins	2	2	6	61
240 or more mins	0	0	1	15
Time not stated	1	0	1	1
Totals	128	127	160	225

During the most recent five-year period, in which the length of time devoted to the operation has been increased, the clinical cure rate has shown a definite and rather striking rise, as indicated in Table X.

TABLE X
RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES ACCORDING TO FIVE YEAR PERIODS

Five-Year Periods	No. of Operations	Operative Deaths		5-Year Local Recurrence		5 Year Clinical Cures	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
I—1915-1919	128	3	2.3%	32	25.0%	34	26.6%
II—1920-1924	127	7	5.5%	24	18.9%	37	29.1%
III—1925-1929	160	8	5.0%	42	26.3%	53	33.1%
IV—1930-1934	225	2	0.9%	48	21.3%	107	47.6%
Totals	640	20	3.1%	146	22.8%	231	36.1%

It cannot be assumed that the steady improvement in the clinical cure rate over this 20-year period is entirely due to the fact that as time has gone by the operative attack has been progressively more thorough. The more careful selection of cases during recent years certainly has also played a part in this improvement in results. In a separate paper devoted to the question of operability we will discuss this matter of the selection of cases in detail.

Biopsy—The question of the harmfulness of biopsy in breast carcinoma has been long debated. At the Presbyterian Hospital it has been the custom

CARCINOMA OF THE BREAST

to do biopsies in all cases where a sure diagnosis cannot be made from the clinical findings. This has included about one-third of the cases. Table XI shows the relationship of biopsy to results.

TABLE XI
THE INFLUENCE OF BIOPSY ON THE RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES

Procedure	No of Operations	5-Year Local Recurrence		5-Year Clinical Cures	
		No	Per Cent	No	Per Cent
No biopsy done	401	102	25.4%	112	27.9%
Biopsy, 6 days or less preoperative	5	1	20.0%	3	60.0%
7 to 12 days preoperative	7	2	28.6%	3	42.9%
13 days or more preoperative	7	2	28.6%	3	42.9%
Biopsy at operation	220	39	17.7%	110	50.0%
Totals	640	146	22.8%	231	36.1%

From these data it is hardly fair to draw any conclusion, because biopsy is more often done in the early than in the advanced cases, and the prognosis is, of course, better in this early group of cases. In order to exclude this disturbing factor we have prepared Table XII, which includes only those cases in which the primary tumor measured more than two centimeters in diameter (pathologic measurements) and yet was operable according to the criteria which today we rely upon. Thus, the earliest, as well as the most advanced cases, have been excluded.

TABLE XII
THE INFLUENCE OF BIOPSY ON THE RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES IN WHICH THE TUMOR MEASURED MORE THAN TWO CENTIMETERS (PATHOLOGIC MEASUREMENTS) AND WAS OPERABLE ACCORDING TO HAAGENSEN-STOUT CRITERIA

Procedure	No of Operations	5-Year Local Recurrence		5-Year Clinical Cures	
		No	Per Cent	No	Per Cent
No biopsy	234	47	20.1%	79	33.8%
Biopsy some days before operation	7	1	14.3%	3	42.9%
Biopsy at operation	123	20	16.3%	61	49.6%
Totals	364	68	18.7%	143	39.3%

From these data it would appear that biopsy does not prejudice the end-results of radical mastectomy. Greenough¹ reached a similar conclusion from his study of the results at the Massachusetts General Hospital. Thus, we do not hesitate to employ biopsy if any doubt regarding the diagnosis remains. If the lesion is clearly a carcinoma and operable we do not, however, biopsy it. Careful study of the clinical features of every case, and an extensive background of experience with lesions of the breast, are necessary if this policy is to be safely pursued. It will be easier and safer for the less experienced to biopsy all breast lesions. There are certain indolent forms of breast abscess, and forms of fat necrosis, which can be clinically indistinguishable from mammary carcinoma. The damage that is done by a radical mastectomy carried out for one of these benign lesions far outweighs the inconvenience of biopsy and the theoretic objections to it.

It is our personal practice to reduce the trauma of biopsy to a minimum by making only a small incision, and excising only a very small wedge of tissue from the superficial part of the lesion. We do not excise the whole tumor, because if this is of considerable size excision will open up tissue planes widely, and possibly increase the danger of spreading the disease.

We find that a small wedge serves adequately for frozen sections in the great majority of cases. If this is not satisfactory we, of course, remove a large piece.

Ward versus Private Cases—It has been the general experience that results are better with private than with ward patients, and this is confirmed by the data in the present series (Table XIII)

TABLE XIII
RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES
Ward versus Private Cases

Classification	No of Operations	Operative Deaths		5 Year Local Recurrence		5-Year Clinical Cures	
		No	Per Cent	No	Per Cent	No	Per Cent
Ward	422	13	or 3 1%	119	or 28 2%	137	or 32 5%
Private	218	7	or 3 2%	27	or 12 4%	94	or 43 1%
Totals	640	20,	or 3 1%	146	or 22 8%	231	or 36 1%

The better results in private patients are no doubt due to the fact that they come for treatment earlier in the course of the disease. This is demonstrated in Tables XIV and XV, which show the duration of the disease and, also, the frequency of involvement of the axilla in ward and private patients.

TABLE XIV
DURATION OF DISEASE ON ADMISSION IN PRIMARY CASES
Ward versus Private Cases

Classification	No of Operations		Duration Less than 1 Month		Duration 1 to 5 Months		Duration 6 Months or More	
	Total	Stated	No	Per Cent	No	Per Cent	No	Per Cent
Ward	422	413	51	12 3%	171	41 4%	191	46 2%
Private	218	182	49	26 9%	65	35 7%	68	37 4%
Totals	640	595	100	or 16 8%	236	or 39 7%	259	or 43 5%

TABLE XV
FREQUENCY OF AXILLARY METASTASIS IN PRIMARY CASES
Ward versus Private Cases

Classification	No of Operations		Disease Limited to Breast		Axillary Metastases	
	Total	Microscopic Report	No	Per Cent	No	Per Cent
Ward	422	409	147	35 9%	262	64 1%
Private	218	213	90	42 3%	123	57 7%
Totals	640	622	237	or 38 1%	385,	or 61 9%

Duration of Disease on Admission—As might be expected, the earlier that patients came for treatment the better was their chance of clinical cure. These data are shown in Table XVI.

There are ready explanations for the two apparent paradoxes in this table. The fact that the results were better in patients who had had their tumors for more than three years than they were in those in whom the duration had been somewhat shorter, can be explained by assuming that the tumors that had been present for such a long time were slow-growing, well differentiated ones, and, therefore, more easily cured. The good results in the group of cases in which the duration of disease on admission was not stated can be explained by the fact that most of these patients with defective histories were private ones, who did better as a group.

Our data are not large enough to provide any significant conclusions.

CARCINOMA OF THE BREAST

TABLE XVI
RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES
ACCORDING TO DURATION OF DISEASE ON ADMISSION

Duration of Disease	No of Cases	5-Year Local Recurrence		5-Year Clinical Cure	
		No	Per Cent	No	Per Cent
Under 2 weeks	50	8	16 0%	27	54 0%
2 weeks to 1 month	50	10	20 0%	17	34 0%
1 to 2 months	110	20	18 2%	44	40 0%
3 to 5 months	126	46	36 5%	45	35 7%
6 to 11 months	119	23	19 3%	34	28 6%
12 to 23 months	75	19	25 3%	20	26 7%
24 to 35 months	27	7	25 9%	6	22 2%
36 months plus	38	6	15 8%	16	42 1%
Not stated	45	7	15 6%	22	48 9%
Totals	640	146 or 22 8%		231, or 36 1%	

regarding the interesting question of whether or not patients with carcinoma of the breast are coming for treatment earlier today than previously

While it is, of course, true, as our data show, that early diagnosis and treatment is one of the most important factors influencing the results in breast carcinoma, there is a considerable group of patients in whom the prognosis is bad even though they come for treatment soon after they discover their disease. This fact is well shown in Table XVII, in which the duration of disease and the presence of axillary metastases are correlated

TABLE XVII
THE RELATIONSHIP OF DURATION OF DISEASE ON ADMISSION IN
PRIMARY CASES TO THE PRESENCE OF AXILLARY METASTASES

Duration	No of Operations		Limited to Breast		Axillary Metastases	
	Total	Microscopic Sections	No	Per Cent	No	Per Cent
Less than 1 month	100	98	49	50 0%	49	50 0%
1 to 5 months	236	229	91	39 7%	138	60 3%
6 months or more	259	253	81	32 0%	172	68 0%
Duration not stated	45	42	16	38 1%	26	61 9%
Totals	640	622	237, or 38 1%		385 or 61 9%	

Axillary Involvement—Among all of the factors influencing the prognosis in carcinoma of the breast treated by surgery that of involvement of the axillary lymph nodes is probably the most important. The relationship of the microscopic findings in the axillary lymph nodes to the end-results in the Presbyterian Hospital series is shown in Table XVIII

TABLE XVIII
RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES ACCORDING TO
AXILLARY INVOLVEMENT (MICROSCOPIC)

Extent of Disease	No of Operations	5-Year Local Recurrence		5 Year Clinical Cures	
		No	Per Cent	No	Per Cent
Limited to breast	237	23	9 7%	145	61 2%
Axilla involved	385	120	31 3%	81	21 0%
No microscopic sections	18	3	16 7%	5	27 8%
Totals	640	146 or 22 8%		231 or 36 1%	

The clinical cure rate is thus seen to be approximately three times as high in those in whom the disease is limited to the breast as it is in those in whom it has extended to the axillary lymph nodes. The frequency of local recurrence appears to be similarly related to the presence of axillary involvement. It is indeed worth while considering the data for local recur-

rence in relationship to axillary involvement in more detail, for they show some interesting features (Table XIX)

TABLE XIX

RELATIONSHIP OF LOCAL RECURRENCE TO AXILLARY INVOLVEMENT (MICROSCOPIC)

Radical mastectomies for which microscopic sections were available	622
I—Disease limited to breast	237 or 38 1%
A—Local recurrence on chest only	17
B—Local recurrence in axilla only	4
C—Local recurrence both chest and axilla	2
Total cases with local recurrence	23 or 9 7%
II—Axillary nodes involved	385 or 61 9%
A—Local recurrence on chest only	84
B—Local recurrence in axilla only	12
C—Local recurrence both chest and axilla	24
Total cases with local recurrence	120 or 31 2%

In the group of cases in which the disease was limited to the breast, recurrence, nevertheless, developed in the axilla in six instances. We can explain this paradox by assuming either that lymph nodes containing the disease were left behind or that the surgeon actually implanted carcinoma in the axilla.

If we could only know before operation whether or not the axillary nodes are actually involved by the disease it would be of considerable help to us in planning treatment. Unfortunately, however, clinical examination is but a poor guide, for the most careful palpation of the axilla frequently fails to detect involved nodes. The experience at the Presbyterian Hospital in this regard is shown in Table XX.

TABLE XX

THE ACCURACY OF CLINICAL DIAGNOSIS OF AXILLARY LYMPH NODE METASTASES IN PRIMARY CASES TREATED BY RADICAL MASTECTOMY

Clinical Diagnosis	No of Operations	Microscopic Sections Available	Axillary No	Metastases Per Cent
Axillary nodes not involved	336	325	143	44 0%
Axillary nodes involved	284	278	236	84 9%
No diagnosis made	20	19	6	31 6%
Totals	640	622	385	or 61 9%

From these data we see that when the clinician thought that there were no axillary metastases he was wrong in 44 per cent of the cases, and *vice versa*, when he thought that the axilla was involved, he was wrong in 15 1 per cent of the cases.

The mere size of the axillary nodes is of considerable value in judging whether or not they contain metastases (Table XXI).

Unfortunately, most of the case records in the present series did not contain measurements of the enlarged axillary lymph nodes expressed in centimeters. We believe that an attempt to measure the transverse diameter of palpable axillary nodes should always be made, even though the surgeon is fully aware of how difficult it is to make such measurements accurately, particularly in obese patients. It is only by the accumulation of actual measurements of this kind that we can hope to become more expert in our judgment of axillary involvement. We have seen only one patient in whom

CARCINOMA OF THE BREAST

TABLE XXI

THE FREQUENCY OF METASTASES IN AXILLARY NODES IN PRIMARY CASES ACCORDING TO THEIR SIZE BY CLINICAL MEASUREMENT

Clinical Measurement of Lymph Nodes	No of Operations	Microscopic Sections Available	Axillary No	Metastases Per Cent
Nodes not palpable	177	171	62	36 3%
Nodes moderately enlarged	359	349	239	68 5%
Nodes massively enlarged	61	60	56	93 3%
Nodes 2.5 cm or more in diameter	23	23	22	95 7%
Not described	20	19	6	31 6%
Total	640	622	385, or 61	9%

enlarged axillary nodes that measured 2.5 cm or more in transverse diameter did not contain metastases

Preoperative Radiation—A small proportion of the patients in this series received preoperative roentgenotherapy. Most of these cases were treated in the years 1915 to 1923, the treatment consisting of several suberythema doses, given over large fields, to the front and back of the chest. We well realize that this is a very different kind of radiation from that given today, but the results are presented for what they are worth. (Table XXII)

TABLE XXII

THE INFLUENCE OF PREOPERATIVE RADIATION ON THE RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES

Treatment	No of Cases	5-Year Local Recurrence		5-Year Clinical Cures	
		No	Per Cent	No	Per Cent
No preoperative radiation	562	126	22 4%	209	37 2%
Preoperative radiation	78	20	25 6%	22	28 2%
Totals	640	146, or	22 8%	231, or	36 1%

When data of this kind are presented, the objection is always raised that results are necessarily better in the group of patients who did not receive radiation because this kind of treatment is administered more often in the advanced cases than in the early ones. This was certainly true in the present series of cases, if the presence of axillary metastases is taken as an index of the extent of the disease. In the group of patients who did not receive preoperative radiation 60.3 per cent had axillary metastases, while in the group radiated preoperatively 72.4 per cent had axillary metastases. In our data we get no closer to an answer to the question by breaking down the cases into different categories, for the numbers of cases then become so small that they have no statistical significance.

It is not our practice today, at the Presbyterian Hospital, to give preoperative radiation to patients with operable carcinoma of the breast. This decision is based upon experience with radiation in patients treated subsequent to 1934, and, therefore, not included in the present report.

Postoperative Prophylactic Radiation—Postoperative radiation, with the intent of preventing reappearance of the disease, was administered more frequently in this series of cases. Indeed, about three-fifths of the patients received it. Many of these patients were treated subsequent to 1923, and received the modern type of radiation. The factors usually were 130 kilovolts, 0.25 Mm of copper and 1 Mm of aluminum filter, tube-skin distance 40cm. The dosage was 400 r over the field of operation on the chest wall.

and anterior axilla, as well as the supraclavicular area and sometimes the opposite axilla. This series of treatments was repeated at least once, after from four to eight weeks. The results of this treatment are shown in Table XXIII.

TABLE XXIII
THE INFLUENCE OF POSTOPERATIVE PROPHYLACTIC RADIATION ON THE
RESULTS OF RADICAL MASTECTOMY IN PRIMARY CASES

Treatment	No. of Cases	5-Year Local Recurrence		5 Year Clinical Cures	
		No.	Per Cent	No.	Per Cent
No postoperative prophylactic radiation	372	73	19.6%	137	36.8%
Postoperative prophylactic radiation	268	73	27.2%	94	35.1%
Totals	640	146	22.8%	231	36.1%

In evaluating these data we again meet with the fact that postoperative prophylactic radiation is more often administered to advanced than to early cases, which prejudices the results. This was, indeed, the case in the present series of cases, for only 53.9 per cent of the patients who did not receive the radiation had axillary metastases, while 72.5 per cent of those who were given postoperative prophylactic radiation had axillary involvement. In order to reduce the disturbing effect of this factor we have prepared Table XXIV, which includes only those cases in which axillary metastases were present, and yet were operable according to the criteria that we today rely upon. Thus, the earlier, as well as the most advanced cases, have been excluded.

TABLE XXIV
THE INFLUENCE OF POSTOPERATIVE PROPHYLACTIC RADIATION ON THE RESULTS OF RADICAL
MASTECTOMY IN PRIMARY CASES IN WHICH AXILLARY METASTASES WERE PRESENT,
YET OPERABLE ACCORDING TO HAAGENSEN-STOUT CRITERIA

Treatment	No. of Cases	5-Year Local Recurrence		5 Year Clinical Cures	
		No.	Per Cent	No.	Per Cent
No postoperative prophylactic radiation	154	34	22.1%	38	24.7%
Postoperative prophylactic radiation	143	40	28.0%	45	31.5%
Totals	297	74	24.9%	83	27.9%

These differences in results in the two groups of cases are not of statistical significance, and we are forced to conclude that this kind of radiation has not been of any demonstrable value in our series.

Palliative Radiation for Recurrence—The usefulness of roentgenotherapy for recurrent disease is quite another matter. It has been of the greatest palliative value in controlling pain due to bone metastases, and in clearing up small local recurrences in the field of operation.

When persistent pain develops in the back, pelvis, or legs of a patient who has had a radical mastectomy for carcinoma of the breast we begin radiation at once, even though the roentgenograms fail to reveal any definite bone lesion.

SUMMARY

In studying a series of 1040 carcinomata of the female breast, seen at the Presbyterian Hospital between 1915 and 1934, inclusive, we have been aided by the punch-card method of analysis, which we heartily recommend for investigations of this sort.

We have stressed the importance of calculating operability and five-year clinical cure rates in *absolute* terms, that is on the basis of the total number of patients seen in the clinic, and without any deductions whatever for patients lost track of, treatment not completed, *etc*. Only in this way can strictly comparable statistics from different clinics be obtained.

A total of 640 radical mastectomies were performed by a variety of methods. Local recurrence in the operative field on the chest and in the axilla was distressingly frequent. It had developed in 22.8 per cent of the 640 patients within five years after operation. Death was usually due, of course, to distant metastases, which developed most frequently in lungs, pleura, and bones.

During the course of the years covered by the present report there was an increasing tendency of the surgeons of the hospital staff to take a longer time to carry out radical mastectomy, and to increase the extent of the dissection. There was suggestive evidence that these more radical operations gave better results.

REFERENCE

- ¹ Greenough, R. B. Early Diagnosis of Breast Cancer. ANNALS OF SURGERY, 102, 233, August, 1935.

LYMPHEDEMA OF THE ARM FOLLOWING RADICAL MASTECTOMY FOR CARCINOMA OF BREAST*

A NEW OPERATION FOR ITS CONTROL

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POSTOPERATIVE LYMPHEDEMA of the arm following radical mastectomy of the breast often proves to be a disabling sequela. The cause of its occurrence has been variably ascribed to (1) Postoperative inflammation (2) Venous obstruction (3) The result of fibrosis following postoperative radiation (4) Recurrent malignancy with obstruction in the axilla (5) The theory proposed by Reinhoff, who ascribes the fibrosis to the dead space left in the axilla when the lateral flap is tented over the axilla in the primary closure. However, he admits that even with closure by primary grafting, which permits skin to remain against chest wall from the very beginning, postoperative lymphedema is not avoided.

Devenish and Jessop, in their paper on the nature and cause of swelling of the upper limb after radical mastectomy, have proved with fair certainty that it is not due to venous obstruction, and that the most likely cause is lymphatic block.

Lymphedema of the arm may prove a very disabling sequela which, in the absence of recurrence, has defied therapy and has, in some instances, driven a patient to amputation of the arm to escape disability and pain. These patients find themselves freer in activity with the arm off than with the heavy weight of a useless appendage.

The methods heretofore used for its relief have been uniformly unsatisfactory. The Kondoleon operations reported, have, on occasion, given slight relief, but these were temporary. Lymphangioplasty has fallen into disuse because of the danger of infection in the lymphedematous tissue, and because, even in the absence of infection, reduction in the size of the arm is not appreciable.

A third, nonsurgical method, suggested by Devenish and Jessop, has given fair results in the less advanced cases. They suggest elevation of the arm and bed rest, for a period of time, to permit recession of the edema and, later, the wearing of an elastic corset about the arm during the day, and elevation during the night.

Ross Veal, in 1937, discussing the problem of postoperative lymphedema following radical mastectomy, wrote "No procedures have yet been devised to remedy it."

* Read before the New York Surgical Society, February 25, 1942

LYMPHEDEMA OF ARM

The following case is presented to call attention to an hitherto untried method to release the lymphedema of the arm following radical mastectomy

Case Report—C R, white, female, age 58 In 1931, eleven years ago, she had had a radical mastectomy performed for a breast carcinoma, followed by radiotherapy Within a year following the operation, swelling of the arm occurred and became progressively greater Her first admission to Montefiore Hospital was in January, 1938, seven years after her operation Roentgenograms taken then, and on many occasions since then, for radicular pain, showed no demonstrable bony metastases, and there is no clinical evidence of recurrence to date

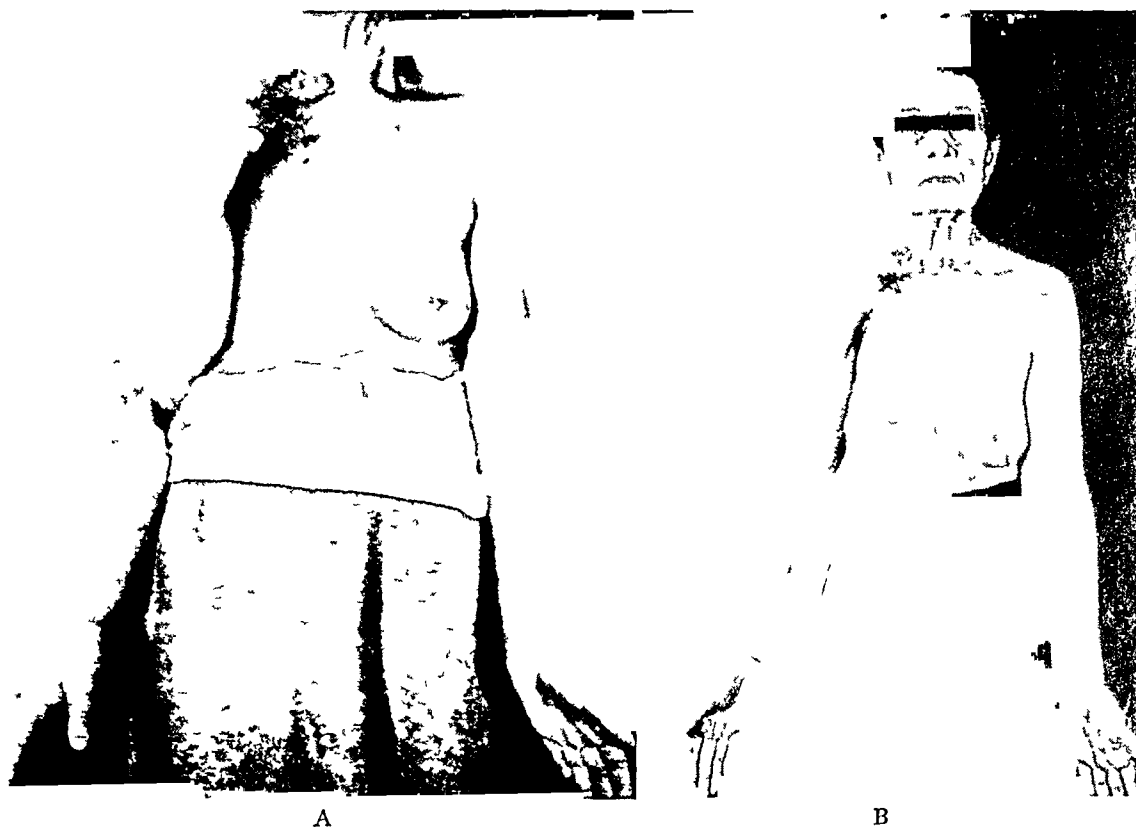


FIG 1—A Appearance of arm nine years after mastectomy for carcinoma of breast B Appearance of arm 12 months after operation

From January, 1938, to January, 1940, she was admitted to the hospital five times with the complaint of swelling, pain, and disability of the right arm During this two-year period she received radiation therapy, regional nerve block, elevation on an airplane splint, and an attempt to transplant a segment of the latissimus dorsi into the axilla The latter attempt had to be abandoned because of the dense fibrosis encountered in the axilla None of these procedures altered the extent of the swelling of the arm or relieved the pain

In October, 1940, she came under our care at Montefiore Hospital The arm and hand were markedly swollen and painful (Fig 1A) The skin was tense, firm, and shiny The arm enlargement forced her to walk with a list to the opposite side to counterbalance its weight

She was unable to turn in bed without lifting the arm, had to lift it to the table with her good arm when she sat down to her meals The hand was swollen The swelling involved the fingers to such an extent that she could not flex them, making the hand a functionally useless appendage

She asked that the arm be amputated for relief. Dr. Venet, Surgical Resident, suggested a plastic procedure. The experimental nature of the procedure was explained to her, and she consented to it on our promise that if it failed we would then amputate the arm. She was put to bed for three weeks, her arm suspended and elevated on a ramp, and an Ace bandage was reapplied each day, as the swelling subsided (Fig 2).

Operation—December 9, 1940. This consisted of the excision of an oval segment of skin and deep fascia, exposing bare muscles, on the medial aspect of the arm. The skin of the chest wall opposite this segment was opened through the deep fascia to the muscles (serratus anterior) covering the thorax (Fig 3), the skin edges were sutured by interrupted silk. The arm was immobilized against the chest wall by a snug bandage.



FIG 2—Appearance of arm after three weeks of bed rest, elevation of the arm, and daily reapplication of Ace bandage in preparation for surgical procedure.



FIG 3—Appearance of arm four weeks after operation.

We intended to carry the incision from arm to chest as a continuous line. The incision was not so extended because of the severe radiation fibrosis of the skin in the axilla. The skin was so leathery in this area, that it would have jeopardized subsequent healing. However, in the absence of such fibrosis, that should be the incision of choice, since it would furnish even greater collateral vascular and lymphatic possibilities than the operation as here performed.

Her postoperative course was uneventful. The wound healed *per primam*. The effectiveness of the procedure may be measured, in part, by her having made no request that we carry out our promise of amputating her arm (Fig 1B). She now walks about freely, can attend to all her wants, has no difficulty feeding herself, she can comb her hair, write, knit, adjust her clothing, and undertake all the activities that she had done previously. Her only limitation is that of abduction of the arm. The arm remains loosely chained to the chest wall (Fig 4).

The principles of the method here presented are more important than

LYMPHEDEMA OF ARM

the details in this case. The use of the chest wall, to furnish a collateral return from the arm, evidently furnishes an adequate return lymphatic flow.

A second operative method, with this principle in mind, is a plastic procedure in which the flap could be swung from the back, across the axilla, and down the arm. This may supply the alternate route for venous and lymphatic return without fixing the arm to the chest wall.



FIG. 4.—Demonstrating mobility of hand with arm fixed to chest wall. Elbow, wrist and finger motion free.

In view of the varied etiologic factors considered in the production of post-operative lymphedema, several prophylactic methods present themselves for consideration:

1. Careful surgery to minimize trauma, and its resultant tissue reaction.
 2. The use of minimum size ligatures to reduce responses to foreign body.
- Silk suggests itself as a good substitute for gut.

3 A careful preparation of the operative field, and protection, during the operation, to minimize the introduction of infection

4 The preservation of available venous channels In such cases, where the axillary vein requires resection, the cephalic vein, which ordinarily is spared in a radical mastectomy, should be particularly guarded against injury

5 Reinhoff's suggestion which consists of swinging a flap of latissimus dorsi to fill the axillary dead space and furnish an alternate route for lymphatic flow

When, despite prophylactic measures lymphedema occurs, and becomes of sufficient severity to produce disability, the operation here suggested adds another surgical procedure for its control

DISCUSSION —DR F W BANCROFT (New York) Dr Guthrie has utilized a simpler technic for some of these instances of edema of the arm He makes, under local anesthesia, several incisions over the shoulder and downward into the upper third of the arm By the use of a clamp, the subcutaneous tissue is tunneled and celloidin ribbon-like bands are inserted, the arm is placed in elevation and the celloidin bands are left in place for about six weeks They are later removed after definite lymphangitic channels have been established I do not believe that he has obtained as beautiful a result as is shown in Dr Standard's case However, it would be my impression that the simplest method should be tried first These marked lymphangitic engorgements of the arm have been more frequent since radiotherapy has been employed, and it is my impression that they are not due to recurrences, as was previously considered the case, nor due to thrombosis of the vein, but are probably the result of sclerosis of the lymphatics coming from the arm into the axilla

EXTRADURAL HEMORRHAGE IN THE ANTERIOR CRANIAL FOSSA

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EXTRADURAL HEMORRHAGE is a frequent cause of death following head injury. Of 507 cases of head injuries which came to autopsy Vance¹ found extradural hemorrhages in 106 cases. In 61, the extradural hemorrhage was the principal cause of death. It is not necessary to describe the course of the usual case of extradural hemorrhage. The syndrome is readily recognized, and the correct diagnosis and operative treatment are most often followed by recovery of the patient. Occasionally extradural hemorrhage is diagnosed clinically but not found at operation. In other cases the diagnosis is missed and an extradural hemorrhage is discovered at autopsy. The failure to find an extradural hemorrhage at operation when the clinical symptoms point to such a lesion is due either to unusual location of the clot or to the presence of some other pathologic process which may simulate an extradural hemorrhage.

This report is concerned with extradural hemorrhage in the frontal fossa. Clots in this location are frequently overlooked at operation unless the surgeon is aware that on rare occasions an extradural hemorrhage may be limited to the frontal fossa. In a perusal of the literature^{2, 3, 4} isolated cases of frontal extradural hemorrhage are alluded to, but the problem itself has received brief consideration. Briesen,⁵ describes the following case: "The clinical picture was classical (of extradural hemorrhage). A bilateral subtemporal decompression was performed in a routine manner. It failed to disclose a hematoma. On autopsy, a large extradural hematoma which had not been diagnosed was found one centimeter anterior to the site of the operation." By far, most extradural hemorrhages are found in the middle fossa, and the usual subtemporal decompression exposure is adequate for the majority of cases. In a series of 504 cases of fracture of the skull studied at autopsy LeCount and Appelbach⁶ found 104 extradural hemorrhages large enough to cause appreciable compression of the brain. Of these, 49 clots covered the convexity of the temporal, parietal and occipital lobes, 14, the occipital lobe, six the frontal and parietal lobes, and 1, the temporal and parietal lobes on both sides.

In the following three cases extradural hemorrhages were limited to the frontal fossa.

Case 1—A white male, age 14, struck the right side of his head on a non stanchion. He suffered a bruise of the right side of the forehead but otherwise had no other symptoms of a severe injury at the time. The accident occurred at 4 30 P M. He went to bed that night feeling well, but awoke at about midnight complaining of severe headache. He vomited several times and then became semistuporous. The

next morning he was still in a stupor, and had involuntary twitching of both sides of the body. That evening, 30 hours after the accident, he was admitted to a hospital. On examination, in addition to the stupor and contusion of the right side of the forehead, the Babinski sign was positive on both sides. Pulse 60, blood pressure 150/90, temperature 101° F. The surgeon at this hospital advised nonoperative treatment. Notwithstanding this the patient was immediately removed to another hospital for operative intervention. When seen at this time (2 A M) the pulse was 54, and there were occasional jerking movements of the face. The right pupil was fixed and dilated, and the Babinski sign positive on both sides. A diagnosis of right extradural hemorrhage was made and immediate exploration carried out. An opening, about five centimeters in diameter, was made in the skull just above the zygoma on the

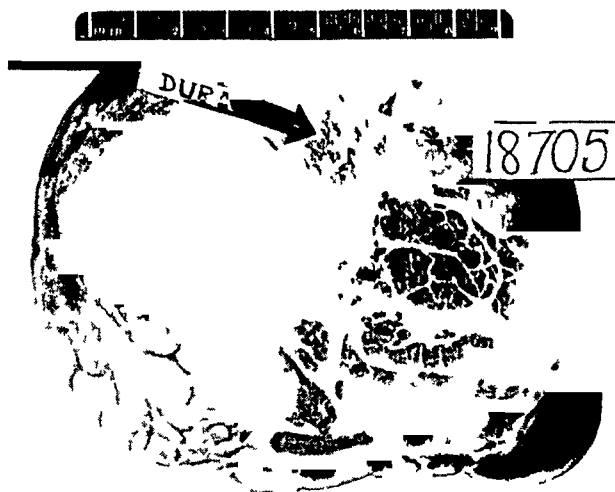


FIG 1—Compression of right frontal pole by extradural clot

right side. There was no evidence of extradural or subdural hemorrhage. A similar exploration was made on the left side without any abnormal findings.

The patient failed to improve, and died 24 hours later. An autopsy disclosed a large extradural hemorrhage, seven centimeters in diameter, in the right anterior fossa. The clot caused marked compression of the anterior portion of the right frontal lobe (Fig 1), with a concave deformity of the lobe. Careful examination did not reveal a fracture of the vault or base of the skull.

In this case the history and findings were so typical of an extradural hemorrhage that thorough explorations of both middle fossae were carried out in search of the clot. The finding of the clot at autopsy, compressing the tip of the frontal lobe, was a new experience to us. In 22 cases of extradural hemorrhage operated upon during the past seven years, all except the three cases herewith reported were found on middle fossa explorations.

Case 2—A white male, age 10, fell from his coaster wagon at about noon. He was not unconscious and went home unassisted. At about 3 P M he began to vomit. Later that afternoon he complained of headache and became drowsy. He was admitted to the hospital at 8 15 P M, about eight hours after the accident.

On examination, there was an abrasion of the left forehead. He was semistuporous. When aroused he seemed bewildered. Percussion of the skull in the left frontal region gave a dull note. The pupils were equal and reacted promptly to light. There

was a ptosis of the left eyelid, a right central facial weakness, and right hemiparesis, with a positive Babinski on the right. The pulse varied between 55 and 64. Roentgenologic examination of the skull showed no evidence of fracture.

A diagnosis of left extradural hemorrhage was made and immediate exploration carried out under local anesthesia. No clot was found in the middle fossa. The usual subtemporal decompression incision was converted into a T-shaped incision to permit exploration of the anterior fossa. An extensive extradural hemorrhage was found compressing the frontal lobe.

The patient made a prompt recovery and was discharged 18 days later.

Case 3—A white male, age 31, was struck over the head with a baseball bat. The exact details are not available concerning his condition immediately after the blow. However, he went home unassisted. The next day he had a headache which was attributed to a "hang-over." However, during the next 48 hours he became drowsy and had difficulty in talking and was admitted to the hospital.

On examination, there was a bruise in the left frontotemporal region. The pulse was 66, blood pressure 140/85. He had some difficulty in naming objects. A right central facial palsy was present. Roentgenologic examination of the skull showed a comminuted, slightly depressed fracture in the left frontal and parietal regions. The patient seemed to improve following a lumbar puncture, and hypertonic glucose solution. His pulse remained slow. The improvement, however, was only temporary. One week after the accident he developed a left internal rectus weakness. The left pupil was larger than the right and failed to react to light. The aphasia became more marked. The following day an exploration for an extradural hemorrhage was carried out. An extensive comminuted fracture was found in the left frontal region. The fragments were slightly depressed. Bright red blood exuded between the fragments. As the bone fragments were removed, a very large, dark extradural clot was found in the anterior fossa.

Following this procedure the patient gradually improved. He became less and less aphasic, so that one month later, at the time of his discharge from the hospital, his speech was almost normal. The left internal rectus weakness was much slower to clear up. Over a period of six months it became less and less marked and finally recovered completely.

DISCUSSION—The location of extradural hemorrhages depends chiefly on the meningeal arteries which are involved. In rare instances extradural hemorrhages result from tears in the intracranial venous sinuses. The middle meningeal is by far the most important vessel concerned in extradural hemorrhage. Nevertheless, the anterior and posterior meningeal arteries may occasionally give rise to extradural clots. The middle meningeal artery is the largest branch of the internal maxillary artery. It enters the skull through the foramen spinosum and is distributed inside the skull to the dura over the frontal, temporal and parietal convexities.

The anterior meningeal artery, which we believe is the vessel injured in anterior fossa extradural clots, is a branch of the anterior ethmoidal artery. The anterior meningeal artery supplies the dura of the floor of the anterior fossa and the dura covering the frontal pole. The posterior meningeal artery is a branch of the ascending pharyngeal artery. Along with a meningeal branch derived from the vertebral artery it supplies the dura of the posterior fossa.

In most reports⁷ concerned with extradural hemorrhage the middle meningeal artery and its branches receive primary consideration, so much so,

that "extradural hemorrhage" and "middle meningeal hemorrhage" are terms which are often used interchangeably. Hemorrhages due to tears of the anterior and posterior meningeal arteries are much less frequent than those due to tears of the middle meningeal artery, but the knowledge that they may occur may lead to the correct diagnosis and treatment in atypical cases of acute cerebral compression following head injuries.

The importance of a fracture of the skull has been unduly stressed in the diagnosis of extradural hemorrhage. The presence of a fracture line crossing a vascular channel is valuable supporting evidence in a suspected case of extradural hemorrhage. The absence of a fracture of the skull has no diagnostic value when other signs and symptoms point to extradural hemorrhage. Of the three cases presented in this report fracture of the skull was found only in one. The incidence of skull fracture in extradural clots due to middle meningeal hemorrhage is about 85 per cent.

Initial loss of consciousness was not observed in Cases 1 or 2. In Case 3, the patient was injured during an alcoholic brawl. It is not known whether or not he was unconscious immediately after the blow to the head. In Cases 1 and 2 semistupor appeared after an interval of a few hours. In Case 3, the patient was drowsy for two or three days after the injury. After that his state of consciousness varied. At times he was more alert, at other times he was drowsy. He never lost consciousness completely.

The pulse was slow in all three patients. Bradycardia has proved to be a valuable sign. Following an injury to the head it frequently indicates cerebral compression either by an extradural or a subdural clot. Elevation of the blood pressure is a less constant finding in extradural hemorrhage. It is a sign which is of value only when present. When the blood pressure increases in a case of extradural hemorrhage, the systolic pressure rises more rapidly than the diastolic, resulting in a high pulse pressure.

The eye signs are of great value. In about 75 per cent of the cases of extradural clot due to middle meningeal hemorrhage, there is a fixed, dilated pupil on the side of the bleeding. In our three cases of extradural hemorrhage in the anterior fossa, eye signs appeared relatively late in the clinical course. In Case 1, the pupils were equal during the first 30 hours, after which the right pupil became dilated and fixed. By this time the patient had generalized twitchings and other evidence of severe cerebral compression. In Case 2, the pupils were small, equal and reacted to light but after a few hours the patient developed a ptosis on the side of the clot. In Case 3, the pupil on the side of the lesion became dilated and fixed to light after an interval of seven days. At the same time a weakness of the internal rectus muscle appeared on the same side.

In addition to the eye signs, findings of lateralizing value were noted in all our three cases. In Cases 1 and 2, there was a bruise of the forehead. In Case 3, there was a bruise in the frontotemporal region and roentgenographic evidence of a fracture of the left frontal bone. Extradural hemorrhages most often occur on the side of the injury, and usually bear some

relation to the site of the blow. Sir Charles Bell, long ago, demonstrated that at the point struck the dura separates from the skull and that bleeding continues into the space of primary separation. In Case 1, bleeding occurred under the site of injury. No other sign of localizing value appeared until 30 hours later, when the right pupil became dilated. At the time little importance was placed on the location of the injury and both middle fossae were fruitlessly explored. In this case bilateral, involuntary twitching and rigidity appeared after an interval of about 12 hours. We have seen twitching and generalized rigidity in other cases of extradural hemorrhage and have learned that they forebode a grave prognosis. In Case 2, a hemiparesis and positive Babinski sign were present on the contralateral side when the patient was first seen at the hospital, about eight hours after the accident. In Case 3, a right facial weakness and an anomia were early signs of focal value. Homolateral eye signs developed much later, after an interval of seven days.

The treatment of extradural hemorrhage is trephine exploration, with the least practicable delay. The side of the injury as indicated by external evidence, roentgenologic and neurologic findings should be explored first. The usual subtemporal decompression exposure is adequate for most extradural hemorrhages, but will not disclose a clot in the anterior or posterior fossa. If the clot is not found in the middle fossa, rapid conversion to a T-shaped incision for exposure of the anterior fossa, should be carried out before exploring the opposite middle fossa. Extradural hemorrhages in the posterior cranial fossa are extremely rare. Coleman and Thomson⁸ have recently pointed out that cerebellar signs in the presence of nuchal rigidity, after a head injury, in a drowsy patient, with a fracture of the occipital bone, should lead to the suspicion of a clot in the posterior fossa. In such a case, recently reported,⁸ an extradural clot was removed from the posterior fossa with gratifying results. The bleeding occurred from a tear in the torcula Herophili.

SUMMARY

Three cases of extradural hemorrhage in the anterior cranial fossa are reported. When the history and findings indicate an extradural hemorrhage, exploration should be undertaken without delay. If the clot is not found in the middle fossa, the anterior fossa should be explored before the opposite middle fossa. An extradural hemorrhage may occur without a fracture of the skull. In extradural hemorrhages of the anterior fossa the eye signs are likely to appear relatively late. In extradural hemorrhages the site of the injury is of great localizing value and should guide the surgeon as to the place of exploration.

REFERENCES

- ¹ Vance, B. M. Fractures of the Skull, Complications and Causes of Death. A Review of 512 Necropsies, and 61 Cases Studied Clinically. *Arch. Surg.*, 14, 1023-1092, 1927.

- ² Wortis, S B, and Kennedy, F Acute Head Injury A Study of 1,000 Cases Surg , Gynec and Obst , 55, 465, 1932
- ³ Gross, S W, and Ehrlich, W Diagnosis and Treatment of Head Injuries, Hoeber, New York, 1940
- ⁴ Gurdjian, E S Studies on Acute Cranial and Intracranial Injuries ANNALS OF SURGERY, 94, 327, 1933
- ⁵ Briesen, Hans V A Head Injury Survey Surg , Gynec and Obst , 71, 633-642, 1940
- ⁶ LeCount, E R, and Appelbach, C W Pathologic Anatomy of Traumatic Fractures of Cranial Bones and Concomitant Brain Injuries J A M A , 74, 501, 1920
- ⁷ Jacobson, W H A Middle Meningeal Hemorrhage Guy's Hospital Reports, 43, 147, 1885
- ⁸ Coleman, C C, and Thomson, J L Extradural Hemorrhage in the Posterior Fossa Surgery, 10, 985, 1941

MASSIVE RUPTURE OF THE LIVER

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MASSIVE RUPTURE OF THE LIVER following traumatic contusion of the abdomen is one of the most serious of abdominal injuries. Most of the cases end fatally within a few hours, due to hemorrhage and shock, a few who do survive the initial hemorrhage die later from bile peritonitis or intestinal obstruction, reported cases of complete recovery are rare. Branch¹ recorded two cases of deep rupture of the liver, with recovery, in 1938, and Krieg,² in 1936, reported one recovery out of ten cases treated during a period of seven years. These three cases are the only instances of recovery from massive rupture of the liver we found in the recent literature.

Rupture of the liver, like rupture of the spleen, is usually the result of trauma. Ordinarily it is met with infrequently (ten cases in seven years at the Detroit City Hospital) but in time of war, particularly in mechanized and air warfare, it is a lesion which may be expected to occur more frequently. In Jolly's³ report of the recent Spanish Republican war he encountered 38 cases of severe liver damage in 238 patients with abdominal wounds.

The attitude of many surgeons faced with a massive rupture of the liver has been one of hopelessness for the general feeling has been that the liver cannot be surgically treated or repaired as other organs, particularly that it cannot be satisfactorily sutured, and that once its vital tissues are extensively injured recovery is impossible, or at least extremely unlikely. It is certainly easy to understand this feeling of hopelessness in view of the available statistics noted above, and the fact that even minor liver wounds are reported to show a mortality of over 60 per cent. The same feeling holds in regard to the spleen, as is evidenced by the routine practice of removing ruptured spleens *in toto* rather than attempting to repair their injury surgically.

We question this feeling of hopelessness concerning reparative liver surgery and believe it is greatly exaggerated, and in many cases may even be contributing to the unnecessarily high fatality from these injuries by failure to attempt simple surgical procedures, such as straightforward suturing, and leading to substitution of unnecessarily complicated and time-consuming surgery, such as fascial or living omental grafts, or, on the other hand, to the use of massive gauze packs which are almost certain to lead to dangerous complications. It must be emphasized that, regardless of the common belief, liver lacerations can be sutured simply and satisfactorily if certain basic principles are kept in mind. In both of Branch's cases extensive lacerations of the liver were readily sutured, and Krieg sutured 15 of the 55 cases of liver laceration which he treated. Further-

more although hemorrhage is invariably serious in liver injuries, few of the patients die of immediate or primary hemorrhage, so that the surgeon usually has a leeway of several hours in which to institute treatment, while secondary hemorrhage after suture of the liver is rare. In view of these facts it seems probable that the mortality from liver injury should not be as high as published statistics would indicate.

One great temptation in massive wounds of the liver is to insert a large gauze pack and then quit. However, the danger of using such large packs cannot be overemphasized, and they usually are entirely unnecessary. It has often been noted that hemorrhage from the surface of a ruptured liver is frequently completely controlled by spontaneous coagulation. Krieg remarked in his report that "in the majority of cases gauze was not inserted into the wound with enough pressure to control hemorrhage and frequently it was merely placed against the wound, yet in no case was there alarming bleeding after the patients had been returned to the ward." The pressure from large gauze packs in the liver area particularly adjacent to the pylorus, is almost certain to result in pyloric obstruction or spasm. Krieg states that in all of the cases in which he used large packs symptoms of obstruction developed, and others have made similar observations clinically and experimentally (Dragstedt,⁴ Walters⁵). On the other hand, the use of a small rubber dam or a cigarette drain leading out from the sutured liver is almost imperative because of the necessity of evacuating pockets of blood and bile and providing drainage of the small bile abscesses which frequently form.

In the case of massive rupture of the liver reported herewith, both the virtues and vices of these details of surgical treatment are illustrated. The ease and simplicity with which the liver can be sutured are strikingly demonstrated, and the trouble which can arise from using gauze packs unnecessarily is equally evident.

Case Report—J S, male, age 26, was admitted to the Newton Hospital, November 21, 1941, immediately after being injured in an automobile accident. He was riding a motorcycle which collided with a car and was thrown over the handlebars to the ground, losing consciousness. When admitted to the hospital he was in severe shock and complaining of extreme abdominal pain. He was conscious and rational. His external injuries were relatively minor including a small laceration over the right eyebrow and multiple contusions and abrasions of the face, both shoulders, anterior chest, left thigh and buttock. There were no visible external injuries of the abdomen, pelvis, lower chest or back. The abdomen, however, was markedly tender and rigid throughout. The patient was obviously in severe pain which was only partially relieved by opiates. His general condition was poor, pulse thready and rapid, blood pressure 70/0, breathing shallow. Shortly after admission he was catheterized and one-half ounce of grossly bloody urine obtained. He stated that he had emptied his bladder completely just a few minutes before the accident. *Clinical Diagnosis* Probable ruptured bladder. An additional diagnosis of probable rupture of the spleen was made because of the evidence of marked intraperitoneal hemorrhage which it was felt was unlikely to be produced entirely by the rupture of an empty bladder.

Operation—After the initial shock had been treated with morphine, intravenous glucose and plasma, the patient's condition was slightly improved and celiotomy, through a midline suprapubic incision, was performed one and one-half hours after admission. There was a large amount of free blood in the peritoneal cavity with many clots, most of which appeared to be coming from the upper abdomen. After removal of the blood, the bladder was carefully examined and found to be intact. A small piece of ragged tissue, one inch in diameter, was found lying free in the pelvis which, on gross examination, was obviously a piece of liver tissue. A large retroperitoneal hematoma could be seen dissecting down along the right ureter.

The suprapubic incision was extended upwards to the xiphoid, passing to the left of the umbilicus. It was later extended two inches laterally to the right, along the right costal margin, to give better exposure of the right lobe of the liver and the right kidney. On exposing the liver fully, a rather startling picture was presented. The liver appeared to be split almost completely in half in the vertical axis of the body, and the two halves were lying separated like an open book, being attached only along the extreme posterior portion. There was only slight active bleeding from the raw surfaces, which were covered with blood clot. On closer examination the rupture in the liver was found to extend down to, but not through, the common duct and hepatic artery. From that point it extended anteriorly just medial to the gallbladder, upwards and posteriorly, just to the right of the falciform ligament, over the dome of the liver, and for a few inches down the posterior aspect of the right lobe. The right and left lobes of the liver were thus connected only by a small bridge of tissue in the region of the common duct and by a portion of the posterior capsule of the liver. The gaping edges of the rupture were fully four inches apart anteriorly.

The temptation was to pack this tremendous laceration with gauze because of the impossibility of approximating the widely gaping edges of the ruptured viscus with sutures. However, it was decided to make an attempt to suture the liver with chromic catgut, placing the sutures deeply and well back from the edges of laceration, on the theory that by so doing some of the larger blood vessels and sinuses with fibrous and muscular walls would be caught in the sutures and might prevent their cutting out. In accordance with this plan, a three-inch, half-curved, cutting needle, with a suture of No. 2 chromic catgut, was placed two inches back from the laceration in the anterior edge of the right lobe, carried straight into the liver for a depth of two inches, and then brought out into the laceration. The needle was pulled through and the suture carried two inches into the left lobe and then out through the anterior edge of this lobe two inches back from the laceration. Two other similar sutures were placed, one halfway between the anterior edge of the liver and the dome of the liver and one halfway between the anterior edge of the liver and the common duct. These three sutures were then tied snugly, whereupon the edges of the laceration were approximated easily and accurately.

After this procedure there was practically no oozing from the liver and the edges remained in contact. Further sutures were not introduced. A gauze pack was placed up to the dome of the liver and another down to the common duct, coming up along the suture line to the anterior edge of the liver. In retrospect, these packs were probably unnecessary, since there was no raw surface exposed and only slight oozing. In view of the complications which developed later it would probably have been better to have used simple rubber dam or cigarette drains.

Following suturing of the liver, the remainder of the liver, the spleen, and the upper abdomen were carefully explored and no other lacerations of the liver or spleen identified, but just below the right lobe of the liver, overlying the right kidney, was a large retroperitoneal hematoma, the size of a grapefruit. This, as noted earlier, could be seen dissecting down the course of the right ureter toward the

pelvis Full exposure was obtained by retracting the colon downwards The posterior peritoneum was then incised, which permitted a mass of blood clot and free blood to escape The kidney was palpated and found to be extensively lacerated Palpation of the kidney started a profuse hemorrhage from the renal artery, which filled the upper abdomen with blood The renal pedicle was immediately grasped between thumb and finger and clamped The pedicle and ureter were divided and the kidney removed The upper pole was found to be lying completely separated from the rest of the kidney and the lower pole was almost completely severed, being attached to the central portion by only a thin bridge of tissue A small cigarette drain was placed down to the renal pedicle and the posterior peritoneum sutured Eight grams of sulfanilamide crystals was distributed through the abdominal cavity The abdominal wound was then closed in layers, bringing the drains out the upper end, two inches below the xiphoid During the operation the patient was given a continuous blood transfusion, which was continued for several hours afterwards, a total of 1200 cc being received Within an hour after operation the blood pressure had risen to 120 systolic

Postoperative Course—The patient made an excellent immediate postoperative recovery In the subsequent treatment special attention was paid to several factors which it was feared might complicate recovery First, a careful examination, including roentgenologic examination, was made as soon as possible, in order to ascertain if other traumatic injuries were present In view of the extensive internal injuries in the upper abdomen, attention was particularly focussed on the possibility of injury to the lungs, ribs or lumbothoracic spine, but none were found In fact aside from lacerations and abrasions of the head and left leg and a mild degree of concussion, the only other injuries were simple fractures of both clavicles

The patient was watched closely for bleeding However, there was only moderate serosanguineous discharge from the drains for the first few days, and never any evidence of active bleeding internally Several blood transfusions were administered to replace the preoperative blood-loss

The question of bile drainage was observed with especial interest, in view of the extensive rupture of intrahepatic bile ducts extending down close to the common duct There was never any evidence of bile peritonitis For the first five postoperative days there was moderate bile drainage from the incision, which stopped entirely on the tenth day The stools remained brown There was no jaundice and the icteric index remained normal Vitamin K was administered subcutaneously daily for one week, as a prophylactic measure

The complications which were especially feared, therefore, did not occur, but two other complications did arise which caused considerable difficulty First, infection During the first three days postoperative there was but little elevation of temperature and it was felt that with the intraperitoneal sulfanilamide the danger of infection had been averted However, on the fourth day, when the temperature rose slightly, and the white blood count remained elevated around 17,000, it was felt advisable to start sulfadiazine by mouth in full doses It would undoubtedly have been wiser to have started it the first day postoperative, as has been our custom in other cases of threatened peritonitis In any event evidence of undrained infection increased, the temperature rose to 102° F, and the white blood count to 37,000 on the tenth postoperative day Exploratory aspiration for subhepatic or subdiaphragmatic collections of pus was unproductive The next day a purulent discharge appeared from the drainage sinus in the upper wound, and three days later the temperature had become normal and the pain, which had been present in the subhepatic area, had disappeared

At this point, the other serious complication arose During the first three postoperative days the patient had vomited occasionally, and it was demonstrated that fluids taken by mouth were not passing through the upper duodenum It was felt

this was due to obstruction from the packing placed against the liver, and when this was removed on the third day the obstruction appeared to have been relieved, so that by the thirteenth day the patient was able to take a full diet without discomfort. However, on the next day, three hours after supper, he suddenly vomited violently most of the food taken that day and, simultaneously, completely disrupted his abdominal incision from the symphysis pubis to two inches below the umbilicus, almost entirely eviscerating his small intestines. The drainage sinus in the upper end of the incision did not give way but poured its purulent discharge down over the eviscerated intestines.

In the process of resuturing the dehiscent incision, palpation of the upper abdomen revealed considerable induration around the drainage sinus, involving the duodenum, but there was no evidence of any undrained pus collection. There was no evidence of any old or recent general peritonitis. The transverse colon had become firmly adherent to the anterior peritoneum adjacent to the drainage sinus. This was freed with some difficulty and the incision was then resutured after eight grams of sulfanilamide crystals had been distributed throughout the lower abdominal cavity.

The patient recovered very quickly from this second operation. He was given sulfadiazine by mouth in full doses, and, after a slight temperature rise up to 101° F for a few days, his temperature reached normal in one week, where it remained. In a few days he again began to retain fluids and soft solids, and had normal brown bowel movements. He was not distended. However, each night he complained of epigastric fullness and vomited six to ten ounces of brown fluid. A small amount of barium was given by mouth at this time (four weeks after his first operation) and showed a partial obstruction in the region of the duodenum, with only a slight residue at six hours. Conservative treatment was followed for another week, but he continued to vomit daily and was unable to maintain an adequate food intake. The vitamin intake was carefully maintained artificially (especially B complex, C and K), and the blood chemistry remained normal—N P N 32, serum protein 8.2% plasma protein 8.1%, and plasma chloride 0.513 mg%. However, the patient continued to lose weight and strength rapidly, and it was decided to perform a jejunostomy for feeding purposes and, if feasible, to free-up whatever obstruction might be present.

Four and one-half weeks after the first operation, therefore, a new incision was made lateral to the left rectus muscle in the upper abdomen. Exploration revealed that the induration around the duodenum had entirely subsided and that the present obstruction was in the upper jejunum. There was evidence of an extensive peritonitis having developed following the second operation, as a result of which several loops of jejunum had become adherent to the under surface of the incision and to each other. These loops were successfully mobilized and jejunostomy performed as planned.

Again, the patient withstood the operation very well. He was started on jejunostomy feedings on his third postoperative day, and fluids by mouth were added on the tenth day. At the end of three weeks he was taking three full meals a day by mouth, and the supplemental jejunostomy feedings were stopped. One week later roentgenograms of the stomach showed no residual after two hours. There was still some dilatation of the second and third portions of the duodenum, but no obstruction. The patient was discharged from the hospital the next day, four weeks after his jejunostomy, and eight and one-half weeks after his injury, with his incisions all completely healed, and with clinically normal liver function.

Subsequent Course—During the six months which have elapsed since his discharge from the hospital this patient has been examined at frequent intervals. He has gained weight rapidly and continues in excellent health, with normal liver, intestinal and kidney function. He returned to work two months after leaving the hospital and, when last heard from, was applying for a job at the Navy Yard, after having been rejected for the Army by his local draft board.

SUMMARY

The interesting features of this case seem to be (1) That such a massive rupture of liver tissue could be so satisfactorily repaired with only three interrupted No 2 chromic sutures (2) It was rather astonishing, but very instructive, to find so little postoperative oozing, and to have such a relatively short period of bile drainage. Apparently, when lacerated liver tissue is accurately approximated the ruptured bile sinuses and blood vessels heal rather rapidly (3) The danger of infection when bile sinuses are opened is well known, but was not sufficiently considered in this case. In all cases of this type it would, undoubtedly, be safer to assume that infection of the lacerated tissue will be present and give maximum treatment with the sulfonamides (sulfanilamide locally, and sulfadiazine by mouth or parenterally) from the beginning (4) The danger of using large gauze packs against the liver was demonstrated in this case, as has been previously noted by others. The packs were undoubtedly unnecessary. At best, such packs are a crude and primitive form of treatment and, although they may at times be a necessary life-saving procedure, they must frequently be considered, as in this instance, a confession of lack of surgical judgment. Finally, to those who may still regard some phases of liver surgery as hopeless, demonstration is herewith afforded that in this instance the patient recovered, and weathered several subsequent serious complications, in spite of a most extensive rupture of the liver complicated by a triple rupture of the right kidney, with its additional, attendant hemorrhage and shock. This fact, incidentally, is of some interest in itself, for in reviewing the literature, there does not appear to be any previously reported instance of recovery of a patient with a massive rupture of the liver complicated by another serious intra-abdominal injury, although several such cases have been reported which ended fatally.

REFERENCES

- ¹ Bianch, C D Injury of the Liver ANNALS OF SURGERY, 107, 475-477, 1938
- ² Krieg, E G Hepatic Trauma Analysis of 60 Cases Arch Surg, 32, 907-914, 1936
- ³ Jolly, D W Field Surgery in Total War Paul B Hoeber, Inc, New York, 1941
- ⁴ Diagstedt, C C Acute Dilatation of the Stomach J A M A, 79, 612, August 19, 1922
- Walters, W Accumulated Bile Displacing Liver Surg, Gynec and Obst, 47, 421, 1928

TEMPORARY OCCLUSION OF THE PORTAL VEIN AND HEPATIC ARTERY

REPORT OF A SUCCESSFUL SUTURE OF AN INCISED
PORTAL VEIN WITHIN THE LIVER

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FEW INSTANCES of successful suture of the portal vein have been recorded Hallopeau¹ sutured a 6 or 7 Mm bullet wound of the anterior surface of the portal vein in a woman, age 35, who had shot herself in the epigastric region with a 9 Mm revolver On admission, her condition was not alarming but a large amount of black blood was found in the peritoneum The opening in the portal vein was closed with one No 0 catgut and several No 16 linen sutures There also was a perforation of the left lobe of the liver, which did not bleed during the operation A drain was inserted There was no jaundice, and the patient was able to leave the hospital in less than 15 days after admission

Giorgi² sutured the liver and an irregular wound of the internal surface of the portal vein of a man who had been shot five times and also had a spinal wound with paraplegia Seven silk sutures were introduced in the vein The patient died about two months later of bilateral purulent pyonephritis The sutured portal vein was pervious Giorgi mentions Schulte's case of suture of the portal vein, injured during operation, as the only other case of direct suture of the portal vein This patient died four days after the operation, but the sutures were found to have held

Romanis³ operated upon a soldier 23 hours after he had sustained a lacerated wound of the portal vein from a fragment of high explosive shell which also had torn the liver A plug was placed in the wound of the liver and two artery forceps were clamped in a longitudinal direction on the vein The plug was withdrawn the second day and the artery forceps removed the third day after operation The patient died of a secondary hemorrhage, but from the right renal artery, on the eighth day

Steindl's⁴ patient, a woman, age 39, apparently lived about 11 months with thrombosis of the sutured portal vein She had during seven hospitalizations a subtotal gastrectomy for ulcer and a cholecystectomy for cholecystitis and cholangitis Finally, in the separation of adhesions in an attempt to perform a choledochohepatostomy, the portal vein, a bile duct and an artery, were torn in two Although the central stump of the portal vein was only one centimeter in length, a very difficult, circular, end-to-end anastomosis, with paraffinized silk sutures, was accomplished After removal of the vascular clamp, blood was observed to pass through the sutured vessel to the liver Six months later the patient was discharged with a

persistent biliary and duodenal fistula, and died 11 months after operation. Necropsy revealed a suppurative cholangitis, abscess of the right lobe of the liver, biliary and duodenal fistulae, and an abscess of the parotid. A portal thrombosis was found which was believed from the symptoms to have started on the ninth postoperative day. From this experience Steindl suggests that in suturing the portal vein clamps should not be used, but that an index finger be passed into the foramen of Winslow to lift the vein forward and control the bleeding during the introduction of sutures.

In the following personal case the patient, at a fifth operation for biliary obstruction, had the portal vein accidentally incised within the liver. This occurred as the hepatic orifice of a biliary fistula was being enlarged. For three days hemorrhage was partly controlled by hemostatic forceps and then, under provisional clamping of the portal vein and hepatic artery, the opening in the portal vein was closed successfully by sutures. Later the biliary fistula which developed was anastomosed into the duodenum. This, and a case of resection of the left lobe of the liver are presented to illustrate the feasibility and possible occasional usefulness of a temporary occlusion of the portal vein and hepatic artery.

CASE REPORTS

Case 1—Mrs. A. B., white, age 38, was admitted to Temple University Hospital, March 5, 1941, with a history of severe attacks of epigastric pain, relieved by morphine, but followed by jaundice, which began two years before and for which she had undergone four operations. The jaundice was associated with intense pruritis, acholic stools and dark-colored urine.

The gallbladder had been removed in May, 1939, with relief for five weeks, when the attacks recurred. The patient returned to the hospital, where she remained for seven months. Reoperation was delayed on account of continued fever. Aspiration and roentgenologic study after air injection was made three times in the fall of 1939 without finding any evidence of a subphrenic abscess. In January, 1940, a second operation and later two additional operations were performed. At the fourth operation a rubber tube was buried in the biliary tract. The patient returned to her home in February, 1940, suffering from mild recurrent attacks of upper abdominal pain which, after five months, became severe, and again were associated with fever and jaundice. In June, 1940, she had returned to the hospital for about a month, in August, 1940, for 20 days, and in October for 15 days. The treatment at these times was mainly dietetic.

On admission, we found the patient jaundiced but fairly well nourished although the mucous membranes were pale. There was a vertical right upper rectus scar and a second depressed oblique scar along the right costal border, extending from the ensiform to the axillary line, both healed.

Laboratory Data Hemoglobin 65 per cent, erythrocytes 313, leukocytes 5,700, P 62, L 28, M 2, E 6, B 2, F 44, NF 18, no abnormal cells, cholesterol 298, icterus index 24 units van den Bergh direct, moderate delay, indirect 0.9, cholesterol esters 162, per cent esters 54, prothrombin specimen clotted. **Urine** Nothing abnormal. **Roentgenologic Study** The intrahepatic biliary ducts of very large caliber, and filled with gas from an abnormal anastomosis with the gastro-intestinal tract (Fig. 1). The liver shadow was well delineated and not enlarged. No rubber tube was detected in the abdomen.

Operation—March 7, 1941. Under spinal anesthesia (procaine 100 mg., pontocaine

OCCLUSION OF PORTAL VEIN

10 mg in 2 L), the subcostal scar was excised, dense adhesions between the anterior abdominal wall, liver, duodenum, stomach and great omentum were separated by sharp dissection. The gallbladder had been removed, the liver, only slightly enlarged, was dark green in color, with rounded edges. When the very adherent stomach was separated from the posterior part of the inferior surface of the liver, a small fistula between the liver and stomach was divided. The opening in the liver, about 4 Mm in



FIG 1—Case 1. Enlarged intrahepatic bile ducts delineated by gas from the stomach entering through a small gastrohepatic fistula.

diameter, was irregular and did not discharge any bile although a trace of bile was observed in the gastric side of the fistula. Probes and small scoops introduced through the opening into the liver removed black, rather soft, irregular calcareous masses, from 3 to 5 Mm in diameter, which evidently had occluded the fistula. The instruments entered very spacious intrahepatic bile ducts. No extrahepatic bile ducts were located. Fused in the dense adhesions, deep and slightly medial to the opening in the liver an elastic tubular structure, about 12 Mm in diameter, was palpated, which apparently entered the liver near its posterior edge. Aspiration of venous blood through a fine hypodermic needle confirmed the impression that this was the portal vein. Upon the vein, also embedded in the adhesions, was a smaller pulsating vessel—the hepatic artery.

With the intention of enlarging the anastomotic channel between the stomach and the intrahepatic bile ducts, a scalpel was introduced into the small opening in the liver and made to cut directly backward, in the belief that the portal vein, on entering the liver, remained to the medial side. Instantly a great gush of blood filled the wound and flowed from the abdomen, which we were unable to remove rapidly enough to permit visualization. Guided by the finger, hemostatic forceps were introduced through the incision in the liver and clamped over the bleeding vein. Not until five Pean forceps had been introduced side-by-side was the hemorrhage arrested. The blood was evacuated from the wound and an attempt made to sew the vein from beneath the forceps. The depth, the intrahepatic location, and especially the mass of artery forceps in the wound made this seem impossible. The opening in the stomach closed with inverting, interrupted, No 36 alloy steel wire sutures, a suction drain introduced, the wound packed with gauze, partly sutured and the patient returned to bed, with a blood pressure of 80/52. An intravenous drip of 5% glucose given during the operation was continued. The operation had consumed 150 minutes. The preoperative blood pressure (108/60) had promptly risen to 120/70 under ephedrine, but fell to 80/54 after 60 minutes, during the period of hemorrhage, but under glucose infusion temporarily rose to 90/60 near the conclusion of the operation. A profuse flow of bile soon appeared through the drains. As the patient reacted, free bleeding occurred from the wound, the systolic blood pressure dropped to 50, and the pulse rate increased to 150. The packing was reinforced, and 500 cc of typed blood transfused.

Postoperative Course—The day following there was no further bleeding, the systolic pressure was 88, and there was but little drainage of bile. Two days after the operation, there having been no recurrence of the hemorrhage, the resident surgeon cautiously opened one of the end hemostats. Blood immediately welled through the dressings and the hemostat was reclamped. This indicated that the patient probably would die of hemorrhage unless we were able to suture the incised portal vein. I could conceive of no way of suturing the vein within the liver substance without fatal loss of blood, except by temporary occlusion of the vessel outside the liver. To attempt to arrest the bleeding by packing through the opening in the liver into the greatly dilated intrahepatic ducts and, possibly, inadvertently, into the portal vein itself, seemed only to spell disaster. Realizing that the portal vein and the hepatic artery were fused in the dense adhesions forming the floor of the wound, it was evident that it would be difficult to liberate the vessel sufficiently, under the five hemostats, to apply a provisional ligature or artery clamp, without an extensive enlargement of the wound and separation of adhesions, which the patient seemed hardly in condition to withstand. It was decided to attempt to locate the vein and artery by the finger and to thrust the blades of a thin-bladed intestinal clamp through the adhesions at each side of the superimposed vessels, with the hope that on closing the clamp the circulation would be arrested without undue traumatism.

Second Operation—March 10, 1941 (three days after the first operation). Under 25 per cent evipal intravenous anesthesia, associated with an infusion of 5 per cent glucose, a test was made to see whether the bleeding would recur if the row of five hemostats were loosened. Cautiously, the Pean forceps at the other end of the row from that which had been loosened the day before was opened—an immediate profuse hemorrhage ensued. This was arrested only partially by reclamping the forceps, the gauze packing was removed quickly from the wound, the portal vein located by palpation, and the thin, springy blades of the intestinal clamp thrust through the adhesions at the sides of the portal vein and hepatic artery, about two or three centimeters distant from the liver. When the instrument was clamped all bleeding ceased and the five hemostatic forceps were removed without further hemorrhage resulting. Three No 0 chromic catgut sutures, passed, in part, rather blindly, through the

overlying layer of liver, were used to close the opening in the portal vein. No hemorrhage followed when the clamp was removed from the artery and vein. A No. 24 F catheter was introduced into the hepatic ducts anterior to the suture line, the wound packed with a single strip of one-inch gauze, and a suction drain introduced to protect the general peritoneal cavity. The blood pressure, which had been 96/86 before beginning the intravenous anesthesia, ten minutes after beginning the operation, fell to 66/36—66/32 for about 15 minutes and rose to 78/38 at the conclusion of the 35-minute operation. It is estimated that 400 to 500 cc of blood was lost during the operation, and this, rather than the estimated 18 minutes occlusion of the vessels, may have been responsible for the hypotension. Apparently, the portal vein had been incised for 10 to 15 Mm, beginning about 5 Mm within the liver substance. Three 4 to 8 Mm gallstones were found in the removed gauze. The wound was malodorous from decomposing blood clot and bile.

Postoperative Course—To our surprise, the patient had a rapid and uninterrupted operative recovery, the highest temperature being 100.6° F. There was no secondary bleeding, the general condition rapidly improved, and much dark turbid bile, changing by March 17 to golden-yellow, was discharged from the aspirating drain and catheter. By May, 1941, the abdominal wound had healed, leaving a small, freely draining biliary fistula in its center. A third operation⁵ was then undertaken to anastomose the organized biliary fistula into the duodenum.

Third Operation—An elliptical excision of the scar was made under a mixed pontocaine and procaine spinal anesthesia. The fistula, which had been delineated by an injection of methylene blue solution, with a wide section of the adjacent rectus muscle, was mobilized, rotated 180° to the left, and anastomosed into the duodenum. Two encircling rows of interrupted No. 36 alloy steel wire sutures were used. The wound was closed with interrupted sutures of wire, and a small drain inserted. On the seventh day the temperature rose to 102° F, the wound was found to be indurated, and was partly opened. This was followed by a temporary discharge of bile, which was succeeded by complete healing. The patient was discharged, symptomless and in good condition, June 17, 1941.

Subsequent Course—On July 6, there was a slight attack of pain in the upper right quadrant, with jaundice noticeable for one day. The jaundice returned, without pain, for one day, on July 20. On August 3, there was an attack of pain lasting three days, with jaundice. Later, attacks recurred about every two weeks, lasting two to four days each time, the pain at times requiring a hypodermic injection. By March 11, 1942, the attacks had become rather infrequent and mild. The patient weighed 142 lbs., 42 lbs. more than when she was discharged from the hospital. The patient was last seen June 19, 1942. There had been a two-day mild attack three weeks before, and a four-day, more severe attack eight days before, the latter with jaundice, clay-colored stools, and chills for three days. The pain had not been severe enough to necessitate a hypodermic in the recent attacks. While the stools, as a rule, are dark, the desirability of better biliary drainage which may require additional operative treatment is obvious.

The possible danger of suddenly interrupting the portal circulation in man deserves very careful consideration. Ligation of the portal vein on the hepatic side of its branches in the rabbit may be followed by death within a few moments. In the dog the systolic blood pressure falls to 40 or 50 within 35 minutes and death has occurred on an average in 45 minutes (D. B. Phemister, in a personal communication, reports that he has recently clamped the portal vein in five dogs with an average survival time of 54 minutes, the extremes being 37 and 100 minutes). If, however, the

portal obstruction is produced after a collateral circulation has previously been established, such as occurs in the experimental animal from the formation of a reversed Eck fistula, then the dog may, for a considerable time, survive the ligation. It is not improbable that a somewhat similar condition exists in man. Although the duration of life from an acute portal obstruc-

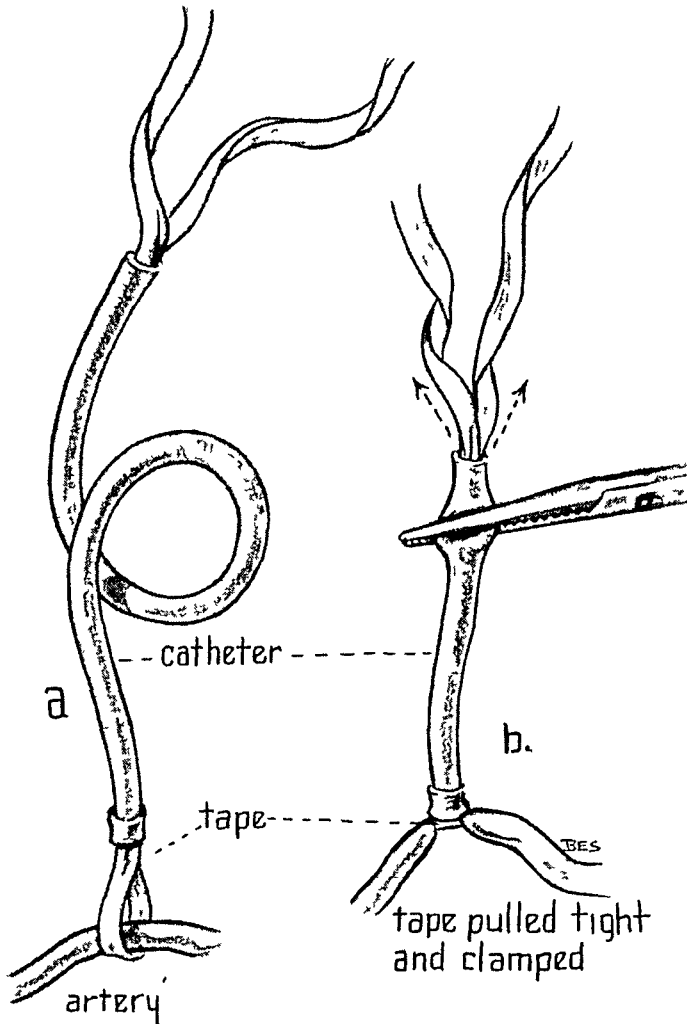


FIG. 2—Simple device used for the temporary occlusion of large blood vessels. The rubber tube may be of sufficient length to be clamped outside the wound.

tion may be longer than in the dog, the period of relative safety remains to be determined. In Case 1, the portal vein and hepatic artery were obstructed for approximately 18 minutes, with recovery. In Case 2, while the obstruction was continued over two hours, during which time the blood pressure fell and then rose from "no registration" to 88 systolic, it is probable that a degree of collateral circulation had been established previous to the operation, due to the growth of a tumor into the vein. Sixteen days before the operation the sudden development of a painful anal edema with the formation of very large internal hemorrhoids suggested a partial portal obstruction,

OCCLUSION OF PORTAL VEIN

In this patient the temporary operative constriction was not considered harmful. In Steindl's case the vein was clamped during a difficult anastomosis. In those patients who have lived with evidence of portal obstruction for days, weeks, months, or longer—and at necropsy show a complete obstruction of the portal vein, as from a thrombus, embolus, pylephlebitis, neoplasm, or injury—it seems reasonable to assume pending further enlightenment, that the patient would not have lived so long had not the obstruction at first been gradual and associated with the development of a collateral circulation. Obviously, the surgeon who temporarily obstructs the portal circulation



FIG 3—Case 2. Choleangiomatous invading all of left and part of right lobe of the liver, removed under temporary occlusion of hepatic artery and portal vein

should be prepared to release the constriction quickly should intense engorgement of the mesenteric veins occur, with an alarming fall in systolic blood pressure. In our two cases mesenteric engorgement may have been present but was not studied and did not attract our attention.

Temporary occlusion of large blood vessels is obtained very conveniently by the use of a tape and section of soft rubber catheter or other fairly stiff rubber tube, as suggested to me by Dr G. Mason Astley (Fig 2). The tape, wet with saline, is carried about the vessel and the ends pulled through the rubber tubing with the aid of a wire loop or fenestrated probe. With traction on the ends of the tape the end of the rubber tube, which may be rolled back, is pushed against the vessel firmly enough to arrest the circulation, when the distal end of the rubber tube may be long enough to hang from the wound, out of the way, and the relatively soft compression of the tape may be released or tightened instantly, as desired. I have used this

simple appliance with satisfaction in anastomosis of the cardiac ends of the divided carotid artery and jugular vein for aneurysm of the thoracic aorta, for end-to-end anastomosis of the cardiac ends of the iliac artery and vein for two aneurysms of the abdominal aorta, and in the following case for the portal vein and hepatic artery to reduce the loss of blood during the excision of the left lobe of the liver for a large cholangioma (Fig 3)

Case 2—A M., white, male, age 55, was admitted to the hospital, April 24, 1941. He had been in good health, except for pneumonia at age 46, until two months before admission, when he developed a soreness in the epigastrium. He immediately consulted a physician and was treated for "muscular strain," with relief in a few days. A week later the pain recurred and extended across the upper abdomen, with muscular spasm. Again, somewhat relieved by rest, he resumed work for two and one-half weeks, when the soreness spread to the lower thorax and left side, and was considered to be pleuritic. Three weeks before admission he became nauseated, with a dull epigastric pain, and a sense of fullness in upper abdomen. The pain has never been severe. He had become constipated, except during the two days before admission, and had lost 20 to 30 pounds in weight. The stools have been dark in color.

Physical Examination—The patient was an emaciated middle-aged white male, apparently not acutely ill. There was a moderate arteriosclerosis, no apparent jaundice, and no ankle edema. There was a large, firm, tender, dull mass in the region of the liver.

Laboratory Data Urine. Specific gravity 1.006, trace of albumin, no sugar, casts or abnormal cells, 67 mg of urobilinogen in 24 hours, Blood pressure 170/110, 14 Gm of hemoglobin, 5,060,000 erythrocytes, 6,550 leukocytes, differential count showed 71 per cent polymorphonuclears, 24 per cent lymphocytes, 1 per cent eosinophils, 2 per cent basophils, filaments 17, nonfilaments 54, no abnormal cells, 35 mg of nonprotein nitrogen, 79 Gm total protein, 4.04 Gm of albumin, 3.3 Gm of globulin, A/G ratio 1.22. Serologic tests for syphilis negative.

On May 7, 1941, with a preoperative diagnosis of malignant tumor of the liver, the abdomen was explored under spinal anesthesia, produced by an injection of 125 mg of procaine, with 12.5 mg of pontocaine, reinforced by the local injection of 180 cc of 1% procaine solution containing 18 minims of 1:1000 epinephrine.

Operation—Through a vertical upper right rectus incision, the left lobe of the liver was found enlarged, from the presence of a diffuse, grayish, rather soft neoplasm. As, from its surface, the right lobe appeared free from disease it was decided to remove the left lobe. The hepatic artery and portal vein were first exposed through an incision in the overlying peritoneum and surrounded by tape, which was carried through a section of rubber tubing and sufficiently tightened to obliterate pulsations in the hepatic artery. Extensive, and quite vascular adhesions to the left lobe were divided and ligated, and the lobe amputated from the right lobe along the line of attachment of the falciform ligament, the round ligament, and through the caudate lobe. Bleeding from the divided liver surface was arrested by transfixion sutures of catgut, by individual ligations and gauze packing. The large left branch of the portal vein, where it entered the left lobe, was found to be filled with soft, grayish nonadherent malignant tissue instead of blood. Many of the larger vessels throughout the lobe, as well as some of those entering the right lobe, also contained tumor substance. The right lobe was also invaded by the neoplasm in places along the line of section. The tape around the two vessels was released near the end of the operation, which consumed two hours and 46 minutes. The patient was then considered to be in fair condition, although the vessels had been occluded over two hours.

The blood pressure before the intradural injection was 125/85, pulse 80, temperature 98.3 F, respiration 16. Ephedrine, 0.045 Gm, was then given subcutaneously. Oxygen inhalation was used during part of the operation. Twenty minutes after the intradural

injection the blood pressure dropped to 70/50. At 35 minutes, the systolic and diastolic pressures were too low to be recorded. About five minutes later the blood pressure had returned to 72/60, ten minutes later to 88/70. The systolic pressure gradually fell after removal of the tape being 50 systolic, at the close of the operation.

The marked fall in blood pressure during the period that the portal vein and hepatic artery were occluded was transient, and resembled that seen in other debilitated patients under spinal anesthesia. On returning from the operating room the blood pressure rose to 130/98 as a transfusion of 500 cc of blood was completed, and a continuous intravenous drip of 5 per cent glucose started. The day of the operation 450 cc of bloody serum was aspirated from the abdominal drain. The day following 350 cc of dark red liquid, the third day 300 cc of dark red liquid, the fourth day 240 cc of bloody liquid, the fifth day 450 cc of bright red liquid, the sixth day 240 cc of dark red liquid, was aspirated from the abdominal cavity. Thus, during the patient's five and one-half-day survival after the operation he lost a total of 2,030 cc of serum and blood. During this period large quantities of parenteral fluid, glucose and blood for replacement, as well as vitamin K, were given.

Pathologic Examination—(Dr Lawrence W. Smith) *Gross* The specimen consists of the left lobe of liver measuring 19 × 14 × 9 cm. The surface is nodular. The capsule is thickened. On section the liver parenchyma cannot be identified. The whole is infiltrated by tumor which is easily expressed. Larger vessels contain tumor, although a few are free. *Microscopically*, several areas present the typical appearance of a primary carcinoma of bile duct epithelial cell origin. The cells are arranged in papillary fashion, tending to form small tubular and acinar structures in an attempt to reproduce bile ducts. The cells, for the most part, are high cuboidal and columnar in character, with ovoid hyperchromatic nuclei placed at the base of the cell. The cytoplasm shows varying degrees of degenerative change. There are many mitotic figures. In places the cells have multiplied and form quite extensive sheets. There is a background made up of what apparently, represents connective tissue derived from the portal areas, in that remnants of persistent bile ducts are found. The cells lining these are in many places hyperplastic and merge with the tumor tissue almost indistinguishably. It is difficult to tell how much of this stroma is residual liver substance and how much is a desmoplastic response. One outstanding feature of the lesion is the invasion of the blood vessels by tumor cells. Owing to the distortion of the entire architecture, it is difficult to state specifically whether these are portal veins or not, but because of their size it seems reasonable to assume that they are. Accompanying this tumor infiltration of the vessels there is an associated thrombosis in many of these vessels. The thrombi are made up of the usual fibrin, leukocytes and red cells and are firmly adherent at various points to the vessel wall, the endothelium of which has been destroyed. Large areas of necrosis are seen. These necrotic areas, apparently, represent tumor tissue as there is a similar shadowy architectural outline of the cells to that making up the viable part of the tumor. This suggests that certain larger branches of the portal vessels have become completely occluded and that this necrosis is primarily the result of infarction. In one of the sections a small amount of liver tissue is recognized, which is being replaced by tumor and the desmoplastic response already commented upon. Hemorrhage and extensive degeneration is universally present in the liver cells and in some places there is a scattering of brownish pigment within the cells suggesting some interference with bile formation.

In summary, the tumor appears to be a primary carcinoma of the bile duct type of epithelium, more commonly known as a cholangioma, and to be distinguished from the primary liver cell carcinoma or malignant hepatoma.

Pathologic Diagnosis Malignant cholangioma of liver

Necropsy—The residual portion of the liver weighs 1,370 Gm, the removed left lobe 1,200 Gm. The portal vein, at the hilum, contains friable neoplastic tissue and

clotted blood, which probably did not entirely occlude the lumen during life. The liver has been divided 3.5 cm to the left of the gallbladder. The left branch of the portal vein is ligated and divided. The bile ducts are patent. The gallbladder is not enlarged and contains thick, dark bile. The lungs contain about a dozen 1 to 2.5 cm metastatic nodules.

SUMMARY

A successful suture of a portal vein, incised within the liver, made possible by a temporary clamping of the portal vein and hepatic artery, is reported.

Five cases of suture or surgical occlusion of wounds of the portal vein are abstracted from the literature.

A practical and simple method for temporarily arresting the circulation in the portal vein and hepatic artery employed in an amputation of the left lobe of the liver for an extensive primary carcinoma is described.

REFERENCES

- ¹ Hallopeau, P. Lateral Suture of the Portal Vein. *Rev de chir, Paris*, 42, 141, July, 1910.
- ² Giorgi, G. Clinical Contribution to Sutures of the Vena Porta. *Policlinico (sez prat)*, 28, 1361, October 10, 1921.
- ³ Romanis, W. H. C. Wound of the Portal Vein. Operation—Death Nine Days Later. *Lancet*, 2, 679, October 14, 1916.
- ⁴ Steindl, H. Circular Suture of the Portal Vein. *Wien klin Wchnschr*, 52, 511, May 26, 1939.
- ⁵ Babcock, W. W. A Simple and Effective Method for the Closure of Biliary Fistulas. *Surg, Gynec and Obst*, 65, 88-90, July, 1937.
- ⁶ von Haberer. Experimental Ligation of Hepatic Artery. *Arch f klin Chir*, 78, 557, 1905.
- ⁷ Petacci, M. On the Surgical Treatment of Primary and Secondary Occlusions of the Vena Porta. *L'Ospedale Maggiore*, 27, 28, January, 1939.

POSTMORTEM PERITONEOSCOPY⁺

A MEANS OF LEARNING PERITONEOSCOPY

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SINCE 1901, when Kelling¹ first demonstrated the possibility of endoscopic examination of the abdomen, peritoneoscopy, by means of ever improved instruments, has been at the disposal of the medical profession. Its value as an aid in diagnosis has unquestionably been established by capable workers, such as Ruddock,² Fry,³ Frank and Starr.⁴ In those conditions in which peritoneoscopy is indicated the method has invariably furnished more concise diagnostic information than any combination of other clinical methods, exploratory celiotomy excepted. It is hard to imagine a reputable hospital, and even a whole city, without access to cystoscopy or bronchoscopy, yet, with respect to peritoneoscopy, a method of equal diagnostic utility, this situation actually exists.

It is interesting to conjecture the reasons for this belated enthusiasm toward peritoneoscopy in contrast to other forms of endoscopy. Although the indications for the use of the peritoneoscope are about equal in the fields of medicine and surgery, its greatest popularity has been in internal medicine. Most surgeons have been trained along lines which cause them to prefer exploratory celiotomy to the less traumatizing peritoneoscopy. The surgeon's desire to touch, as well as observe abdominal pathology makes him reluctant to employ what he considers to be temporizing procedure with peritoneoscopy. On the other hand, medical men, with more surgical conservatism, have made wider use of the peritoneoscope. Perhaps an outstanding reason why peritoneoscopy has found few devotees is that sufficient training in the use of the instrument might be expected to require years if gained on living subjects drawn from one's private practice or chance hospital cases. One's diagnostic ability with the peritoneoscope naturally increases with experience. The problem narrows itself down to the desirability of acquiring experience with the instrument by having performed a substantial series of peritoneoscopies.

One of the chief objectives in this report is to point out the fact that valuable experience may be readily gained in the autopsy room if one will peritoneoscope several dead bodies just previous to the routine autopsy. Probably no other form of endoscopy lends itself so well to cadaver practice. In the 500-bed Episcopal hospital, 298 autopsies were performed in a 12-month period, 1940-1941, constituting 74 per cent of all deaths. Out of

* The observations detailed in this communication are the results of examinations made by the author while Resident Pathologist at the Episcopal Hospital, Philadelphia, Pa.

this group, during a period of nine months, 100 bodies were peritoneoscoped just previous to the routine autopsy. The group included 53 males and 47 females, varying in age from eight months to 85 years. The interval after death at which the examination was performed ranged from one-half hour to 48 hours, the average being eight hours. This study endeavored to make the following contributions to the field of peritoneoscopy, namely:

- I The value of postmortem peritoneoscopy, both to the beginner and to the experienced operator interested in greater accuracy
- II The percentage-chance of seeing various abdominal viscera through the peritoneoscope
- III List of pathologic processes observed in 100 unselected bodies
- IV Comparison of clinical with peritoneoscopic accuracy in this series

I THE VALUE OF POSTMORTEM PERITONEOSCOPY

(1) No danger, as in the living

(2) Technic of inserting the instrument can be mastered. This is important because of the variations from normal existing in different abdominal walls. It is surprising how one's estimation of the thickness of the abdominal wall may be incorrect. As entrance into the abdomen is a blind procedure, one's sense of touch with the scalpel, or pneumoperitoneum needle and trocar, in judging entrance into the peritoneal cavity, is all important, because this is the step when the majority of reported accidents have occurred. Confidence, and an educated sense of touch, may be readily acquired in the morgue.

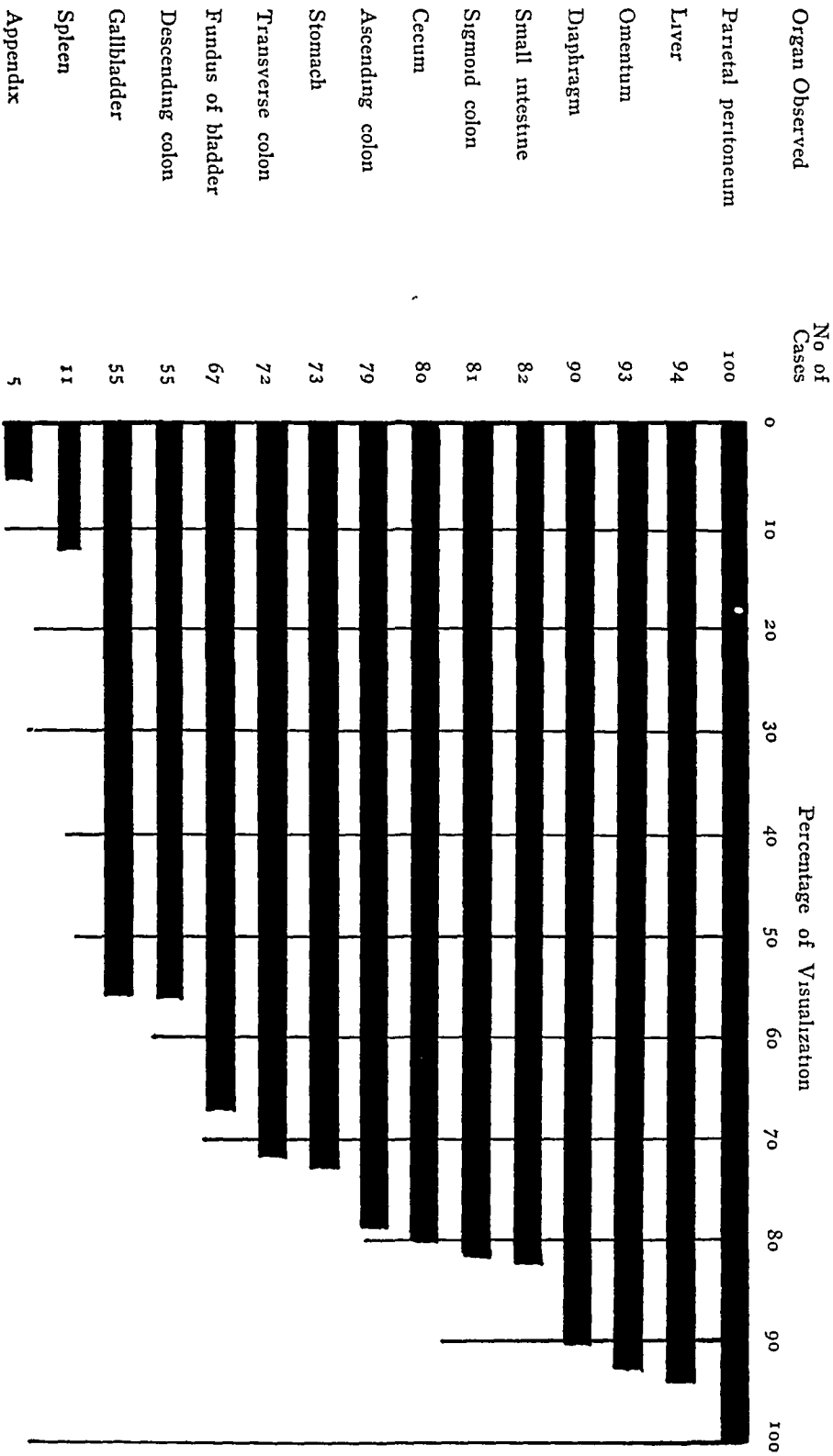
(3) Plenty of time to study individual cases

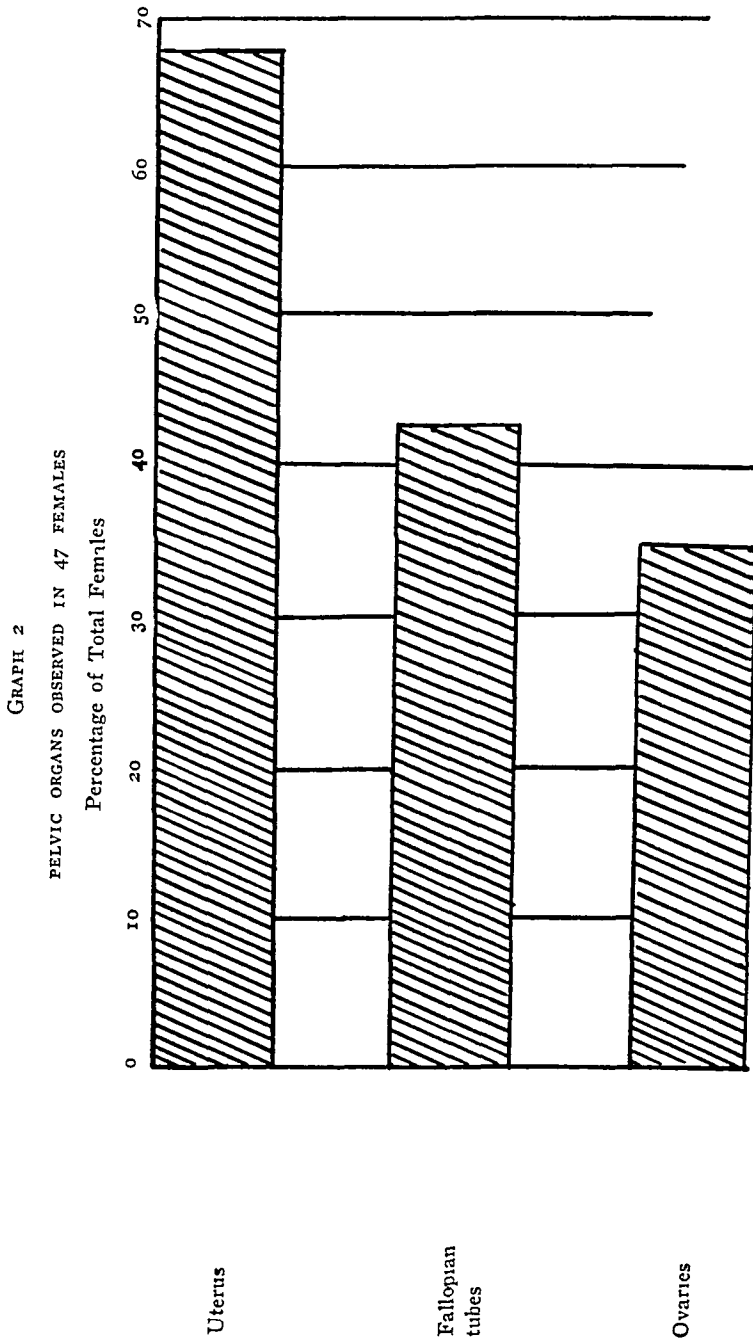
(4) Opportunity to observe normal as well as abnormal abdominal cavities. Although visual representation with the peritoneoscope is marvelously accurate, the impression gained is very different from exploratory celiotomy. Through the peritoneoscope, the peritoneal cavity is seen as a closed space, where orientation is more confusing. The wide variations in contour, size, and color of normal viscera must be appreciated if one is to analyze and evaluate pathologic processes with the peritoneoscope.

(5) Immediate postmortem check of peritoneoscopic impression. The value of this is obvious and, of itself, worthy of recommending postmortem peritoneoscopy, especially to the beginner. In this series of 100 cases accuracy of interpretation was much greater in the last 50. What man doing peritoneoscopy has not, on occasions, wished to really know if his diagnosis was correct? Such errors in this series as misinterpreting large intestine for a distended gallbladder, or an ovarian cyst for a loop of small intestine, would have gone unrecognized but for autopsy inspection. Every physician who reports a higher percentage of diagnostic accuracy with the peritoneoscope, as against clinical means, should verify as many of his diagnoses as possible with autopsy or exploratory celiotomy. Only in this way will he convince himself and his colleagues of his accuracy.

(6) Opportunity to practice "positioning" the patient. This applies to putting the body in Trendelenberg and Fowler's positions as well as rotating

GRAPH I
PERITONEOSCOPIC VISUALIZATION OF ORGANS COMMON TO BOTH SEXES IN 100 BODIES





it to either side in order to better visualize organs in less accessible locations, particularly female pelvic organs, appendix, gallbladder, stomach and spleen

(7) As a substitute for routine autopsy In the rare instance when permission for autopsy cannot be obtained, the family may consent to examination of the abdomen by the peritoneoscope, and thus valuable information may be obtained for the clinician

(8) Opportunity to practice biopsy technic and other forms of experimental peritoneoscopy

II PERCENTAGE-CHANCE OF SEEING ABDOMINAL VISCERA

In most articles on peritoneoscopy a list of the abdominal viscera possible to visualize is given, but, it goes without saying, that not all of these organs will be seen in every case It seemed of value to record the organs observed in each subject, and thereby fairly well estimate the percentage-chances of seeing certain organs In Graph 1, in which are listed organs common to both sexes in 100 unselected cases, one notes a wide variation in the success with which various viscera were visualized Thus, the liver was observed in 94 instances (94 per cent), while the appendix was seen in only five All the organs except the spleen and appendix were noted in 55 per cent of cases, or over It is felt that this represents a fair cross-section of average cases and coincides with data obtained from 30 cases of peritoneoscopy performed on living patients in this institution Although the appendix was carefully sought for in all cases, in the last 25, in which the body was tilted to the left side, the organ was visualized three times as frequently as when this position was not assumed

In general, it is true that a spleen of normal size is not visible with the peritoneoscope, however, in this series, of the 11 observed, the smallest weighed 90 and the largest 500 Gms Seven visible spleens weighed less than 150 Gms These were encountered with the body in Fowler's position and rotated to the right

Graph 2 represents the percentage of female pelvic organs visible in 47 females That this is not a fair cross-section of female pelvic organ visibility is appreciated from the fact that most of these bodies were those of women over 50 years of age, in whom uterine retroversion and senility were prominent features

III LIST OF PATHOLOGIC PROCESSES OBSERVED IN 100 UNSELECTED BODIES AND

IV COMPARISON OF CLINICAL WITH PERITONEOSCOPIC ACCURACY IN THIS SERIES

Tables I to IV list the pathologic processes considered in this study The first column to the left lists the processes considered, whether they were actually present or not The second column, "Times Diagnosis was Considered," totals the clinical and peritoneoscopic opinion before autopsy The third column is the number of times the pathology was actually found at

TABLES I TO IV

TABULATIONS OF THE PATHOLOGIC PROCESSES OBSERVED PERITONEOSCOPICALLY IN 100 UNSELECTED BODIES, AND A COMPARISON OF THE CLINICAL WITH THE PERITONEOSCOPIC ACCURACY IN THIS SERIES

TABLE I

Pathologic Process Miscellaneous	Times Diagnosis Was Considered	Post- mortem Confirm- ation	Diagnosis Made Where Pathology					
			Existed		Was Absent		Errors	
			Clinical	Scope	Clinical	Scope	Clinical	Scope
1 Normal abdomen	29	24	18	24	2	3	8	3
2 Adhesions	22	22	6	22	0	0	16	0
3 Ascites	9	8	3	8	1	0	6	0
4 Hernia inguinal	19	19	8	17	0	0	11	2
5 Hernia femoral	1	1	0	1	0	0	1	0
6 Epiplocele	3	3	0	3	0	0	3	0
7 Generalized carcinoma	5	1	1	1	4	0	4	0
8 Generalized sarcoma	2	2	0	2	0	0	2	0
9 Miliary tuberculosis	1	1	1	1	0	0	1	0
10 Tuberculous peritonitis	1	0	0	0	1	0	1	0
11 Undescended testis	1	1	1	1	0	0	0	0
12 Peritonitis	4	4	0	4	0	0	4	0
13 Pneumoperitoneum	1	1	0	1	0	0	1	0
14 Hematoperitoneum	3	3	0	3	0	0	3	0
15 Subperitoneal purpura	2	2	1	2	0	0	1	0
16 Acute pancreatitis	1	1	0	0	0	0	1	1
17 Suspected mass	4	0	0	0	4	0	4	0
18 Retrocecal abscess	1	1	0	0	0	0	1	1
19 Mesenteric thrombosis	1	0	0	0	1	0	1	0
Totals	110	94	39	90	13	3	69	7

TABLE II

			Diagnosis Made Where Pathology							
			Existed		Was Absent†		Errors			
Pathologic Process			Clinical Scope		Clinical Scope		Clinical Scope			
Gastro-Intestinal Tract										
1	Carcinoma of stomach	5	1	0	0	3	0	4	1	
2	Ptosis of stomach	2	2	0	2	0	0	2	0	
3	Gastro-intestinal malignancy	4	1	1	0	3	0	3	1	
4	Diverticulosis	7	7	0	4	0	0	7	3	
5	Ruptured appendix	1	0	0	0	1	0	1	0	
6	Appendix in hernia	1	1	0	1	0	0	1	0	
7	Perforated bowel	1	1	0	1	0	0	1	0	
Totals			21	13	1	8	7	0	19	5
Spleen										
1	Splenomegaly	2	2	2	2	0	0	0	0	
2	Chronic perisplenitis	2	2	0	2	0	0	2	0	
3	Acute toxic splenitis	1	1	1	1	0	0	0	0	
Totals			5	5	3	5	0	0	2	0

TABLE III

Pathologic Process		Times Diagnosis Was Considered	Post- mortem Confirm- ation	Diagnosis Made Where Pathology					
				Existed		Was Absent		Errors	
				Clinical Scope		Clinical Scope		Clinical Scope	
				Clinical	Scope	Clinical	Scope	Clinical	Scope
Liver									
1	Chronic passive congestion	19	19	15	19	0	0	4	0
2	Portal cirrhosis	11	9	3	9	2	0	8	2
3	Fatty metamorphosis	5	5	2	5	0	0	3	0
4	Chronic perihepatitis	11	11	0	10	0	0	8	2
5	Hepatomegaly	5	3	3	4	1	1	1	2
6	Hemangioma	3	3	0	2	0	0	3	1
7	Metastatic carcinoma	2	1	1	0	1	0	2	1
8	Cholangioma	1	1	1	1	0	0	0	0
9	Amyloidosis	1	1	1	1	0	0	0	0
10	Acute yellow atrophy	2	1	0	1	1	0	2	0
11	Subacute yellow atrophy	1	1	1	1	0	0	0	0
Totals		61	55	27	53	5	1	31	8
Gallbladder									
1	Distended gallbladder	8	7	2	7	0	1	5	1
2	Cholelithiasis	11	10	3	2	0	2	7	10
3	Chronic cholecystitis	4	3	0	3	1	0	4	0
4	Pericholecystic abscess	3	3	1	2	0	0	2	1
Totals		26	23	6	14	1	3	18	12

TABLE IV

Pathologic Process	Times Diagnosis Was Considered	Post- mortem Confirm- ation	Diagnosis Made Where Pathology				Errors	
			Existed		Was	Absent		
			Clinical Scope		Clinical	Scope	Clinical	Scope
			Female Pelvis					
1 Uterine retroversion	12	10	2	2	0	3	8	11
2 Absent uterus	5	2	2	3	0	2	0	3
3 Uterine fibroid	7	4	0	3	1	1	5	2
4 Sarcoma of uterus	1	1	0	1	0	0	1	0
5 Pelvic malignancy	1	0	0	0	1	0	1	0
6 Absent uterus and adnexa	1	1	0	1	0	0	1	0
7 Hydrosalpinx	3	3	0	2	0	0	3	1
8 Ovarian cyst	7	6	0	4	0	1	6	3
9 Chronic salpingitis	3	3	0	3	0	0	3	0
10 Absent fallopian tube(s) and ovary	2	2	2	2	0	0	0	0
11 Varicosities of ovarian vein	2	2	0	2	0	0	1	1
12 Lithopedion in oviduct	1	1	0	0	0	0	1	1
Totals	45	35	6	23	2	7	30	22

TABLE V

SUMMARY OF TABLES I TO IV

Pathologic Process By Section	Times Diagnosis Was Considered	Post mortem Confirm- ation	Diagnosis Made Where Pathology				Errors	
			Existed		Was Absent			
			Clinical Scope		Clinical Scope		Clinical	Scope
			Clinical	Scope	Clinical	Scope	Clinical	Scope
1 Miscellaneous (Table I)	110	94	39	90	13	3	69	7
2 Gastro-intest tract (Table II)	21	13	1	8	7	0	19	5
3 Spleen (Table II)	5	5	3	5	0	0	2	0
4 Liver (Table III)	61	55	27	53	5	1	31	8
5 Gallbladder (Table III)	26	23	6	14	1	3	18	12
6 Female pelvis (Table IV)	45	35	6	23	2	7	30	22
Grand Totals	268	225	82	193	28	14	169	54

autopsy The next four columns specify the number of times the diagnosis was made clinically and by peritoneoscopy, both when the pathology was present and when absent The last two columns on the right compare the errors It is considered an error if a diagnosis was made either clinically or by peritoneoscopy when the pathology was actually not present For example, a diagnosis of generalized carcinomatosis was made in five bodies, and was actually present in only one Four of these diagnoses were made clinically, when, actually the condition was not present, and the peritoneoscope disproved it in these four cases The one case in which it was actually present was diagnosed correctly both by peritoneoscopy and clinically The total errors then were Clinical—4, peritoneoscopic—0 The errors for each method are calculated as follows Take the difference between "Postconfirmation" (column 3) and "Times Diagnosis made where Pathology Existed" (columns 4 or 5), and add this to the corresponding group under "Diagnosis made where Pathology was absent" (columns 6 or 7) This total is the number of cases in which error was made by each method

The tables include all the pathologic processes which came into view of the peritoneoscope in 100 postmortem cases, and no attempt has been made to limit it only to significant things which would have been of value as a peritoneoscopic diagnosis before death The lessons learned from this study the more important of which have been enumerated, were both varied and highly instructive

A word about technic The Ruddock peritoneoscope and method were used, the bladder being catheterized in all cases before study The degree of rigor mortis present in the abdominal musculature, even up to 48 hours, did not appreciably interfere with visibility It was also found that a darkened room was not essential as one's eye soon learns to concentrate on the peritoneoscopic field, just as the microscopist's eye does on the microscopic field If the effect of a darkened room is desired, however, a black sheet may be draped over the observer's head

REFERENCES

- ¹ Kelling, G Über Esophagoskopie, Gastroskopie und Koloskopie Read before the 73rd Versamml Deutsch Naturforscher and Ärzte, Hamburg, September 23, 1901 Munchen med Wchnschr, 57, 2358, 1910
- ² Ruddock, John Peritoneoscopy Analysis of 900 Cases Examined Gynecology & Obstetrics, Vol III, Chapter 16, P 1-51 W P Prior & Co Revised to 1941
- ³ Fry, K E Peritoneoscopy Surg Clin of North Amer, 20, No 6, December, 1940
- ⁴ Starr, A, and Frank, H The Present Status of Peritoneoscopy Inter Abst of Surg, 73, 423, 1940

RÔLE OF INFECTION IN THE PATHOGENESIS OF LIVER NECROSIS IN HYPERTHYROIDISM

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THE IMPORTANCE of alteration of liver structure and function in hyperthyroidism has been frequently emphasized. That liver function is impaired in most instances of hyperthyroidism has been definitely evidenced in the results of clinical tests^{1, 2}. On the other hand, structural changes observed in the liver have been for the most part chronic in character and only rarely acute^{3, 4, 5}. The question then is raised of the significance of this liver damage when it does occur, and of its relation or dependence on the state of hyperthyroidism. Means⁶ has suggested that the structural changes are not a part of the syndrome of hyperthyroidism but are probably related primarily, if not entirely, to secondary factors. This possibility is supported by the work of Haban⁷ who observed the occurrence of liver damage in rabbits fed desiccated thyroid when infection was present, but not when such secondary factors were absent. This finding was recently substantiated in this laboratory⁸ in a study of hyperthyroidism in rabbits infected with the Shope papilloma.

In a further study of this question to determine the factor or factors in the skin papilloma of rabbits that resulted in liver necrosis when combined with hyperthyroidism, the following experiments were carried out. Eleven normal rabbits were given intradermal injections of hemolytic *Staphylococcus aureus* in such a manner that large areas of infection developed in the skin. Eleven other normal rabbits were given toxic doses of desiccated thyroid in addition to skin infection with hemolytic *Staphylococcus aureus*. In the first 11 rabbits no necrosis of the liver was found, but in the second group, 10 of the 11 showed marked necrosis of the liver.

To correlate the experimental data with clinical findings, eight autopsy cases on file in the Duke Hospital Department of Pathology were studied. Two of the eight cases showed acute changes in the liver and there was suggestive evidence that this change was due to the combination of acute infection and severe hyperthyroidism.

In the experiments, normal domestic rabbits were used, each kept in a separate cage, and fed an excess of a balanced diet. Hyperthyroidism was induced by the daily oral administration of 0.768 Gm of Armour's desiccated thyroid, U S P. In a previously reported experiment⁸ this amount had been found sufficient to produce death in 7-15 days in normal rabbits with signs of toxicity, as indicated by the weight-loss, developing about 48 hours after the administration of the first dose.

The virulent strain of hemolytic *Staphylococcus aureus* used was isolated from an abscess occurring spontaneously in a rabbit and was subcultured daily on blood agar slants. The organisms for the inoculations were obtained from one blood agar slant and suspended in a constant amount of normal saline. Up to subculture eight, the organisms retained their original virulence, however, after this it was necessary to pass through rabbits again. Daily inoculations of one to two cubic centimeters of the suspension was made in the skin of the back. Within 24 hours after the first inoculation an area of inflammation developed at the injection site and, in some instances, rapidly spread by the lymphatics to the abdomen. The lesions were graded as one plus to show a localized area of cellulitis, two plus to denote beginning spread to the abdominal skin, three plus to indicate involvement of the abdominal skin, and four plus to show widespread induration of the entire abdomen.

TABLE I
CONTROL RABBITS HAVING ACUTE HEMOLYTIC STAPHYLOCOCCUS INFECTIONS

No of Rabbit	No of Days of Infection	Grade of Infection	Survival Period in Days	Weight-Loss in Grams	Degree of Liver Necrosis
4	3	++++	3	350	0
7	3	++++	3	350	0
8	3	++++	3	350	0
12	5	++++	5	325	0
14	6	+	6	250	0
			(killed)		
15	6	++	6	300	0
			(killed)		
16	6	++	6	150	0
			(killed)		
21	2	++++	2	375	0
22	1	++++	1	150	0
23	5	++++	5	375	0
24	5	++++	5	375	0

The 22 rabbits used were divided into two groups. In Group I there were 11 animals given daily injections of the suspension of virulent hemolytic *Staphylococcus aureus*. With the exception of three animals that received relatively avirulent organisms, death resulted in three to five days, apparently from the severe infection. The data is summarized in Table I. Group II

TABLE II
DESICCATED THYROID FED RABBITS HAVING ACUTE HEMOLYTIC STAPHYLOCOCCUS AUREUS INFECTIONS

No of Rabbit	Amount of Desiccated Thyroid per Day in Gm	No of Days Receiving Desiccated Thyroid	No of Days Infection	Grade of Infection	Survival Period in Days	Weight-Loss in Grams	Degree of Liver Necrosis
5	0.768	4	2	+++	4	450	++++
9	0.768	5	2	++++	5	425	+++
10	0.768	9	6	+	9	600	++
11	0.768	5	3	+++	5	400	+
13	0.768	7	5	+	7	825	++++
17	0.768	3	1	++++	3	150	++
18	0.768	4	2	++++	4	600	++++
19	0.768	4	2	++++	4	250	++++
20	0.768	3	1	++++	3	425	0
25	0.768	6	4	+++	6	600	+++
26	0.768	5	3	++++	5	250	++++

consisted of 11 rabbits given daily doses of desiccated thyroid in addition to inoculations with hemolytic *Staphylococcus aureus* as in Group I. The administration of the desiccated thyroid was begun two days before inoculations were started. The pertinent data for Group II is shown in Table II.

None of the animals in Group I showed any significant liver change. On the other hand, necrosis of the liver was found in 10 of the 11 animals in Group II. This necrosis varied from small focal and central areas to as

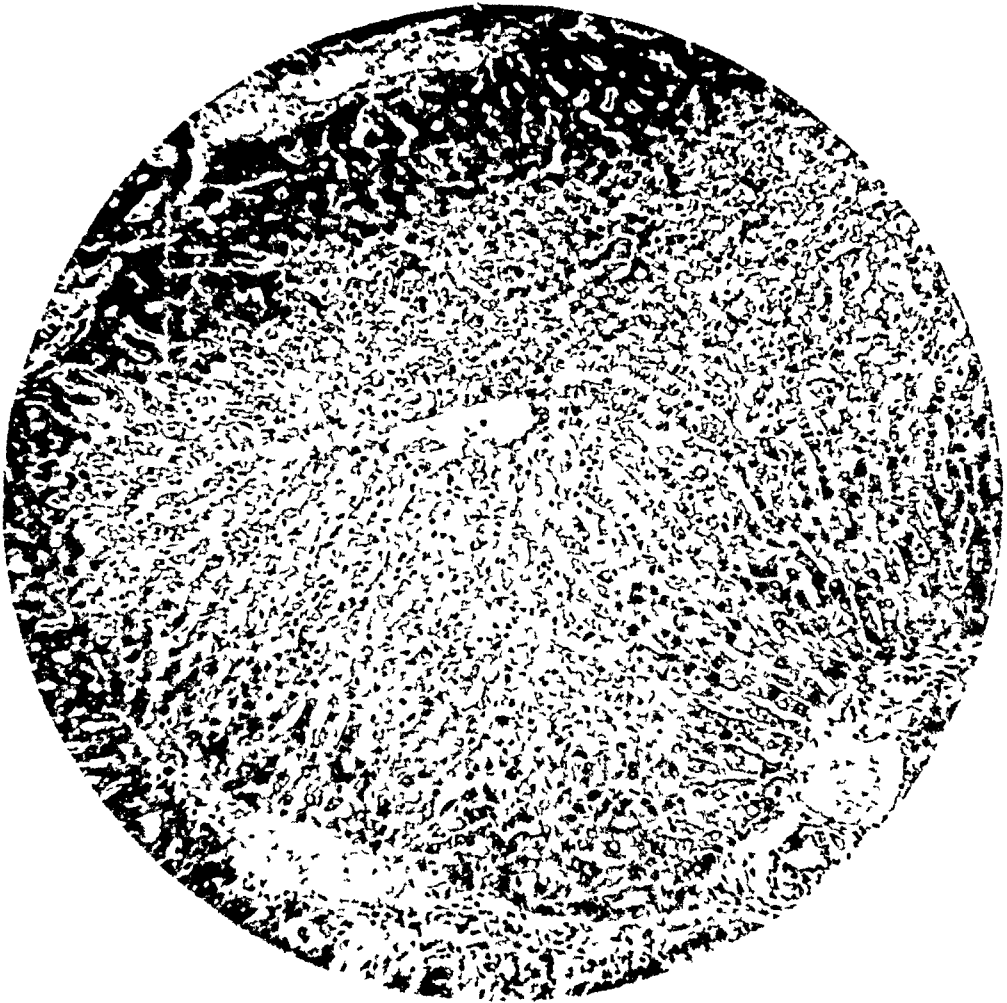


FIG. 1.—Rabbit No. 11. Photomicrograph showing central necrosis of the liver in rabbits from the combination of hyperthyroidism and acute hemolytic staphylococcus infection ($\times 150$).

much as three-fourths of the liver lobule (Figs. 1 and 2). The single animal not showing necrosis survived only 24 hours after the first inoculation with hemolytic *Staphylococcus aureus*.

In a previous report⁸ from this laboratory it was demonstrated that necrosis of the liver does not occur in normal rabbits given desiccated thyroid until death resulted.

With this definite experimental evidence of the responsible factors of the acute liver lesions in hyperthyroidism, the autopsy cases, collected by the Duke Hospital Department of Pathology, were studied to determine if liver

necrosis existed in acute hyperthyroid reactions and, if present, what was its relation to other factors. The material represented eight cases of hyperthyroidism. Of these, seven died from an acute hyperthyroid reaction, while the remaining one died as a result of a pulmonary embolus on the 14th day after operation and did not have an immediate severe postoperative reaction.

The findings in this group of cases are summarized in Table III where the degree of acute and chronic damage to the liver is classed as one plus,

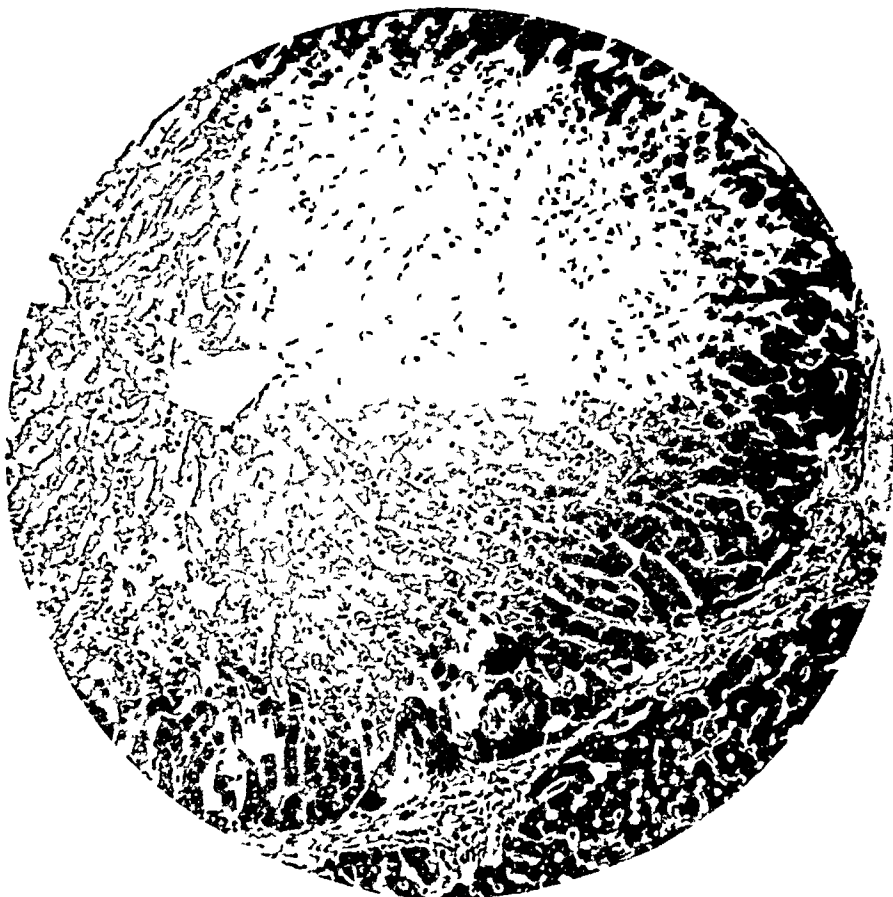


FIG. 2.—Rabbit No. 9. Photomicrograph showing more severe grade of central necrosis in liver of rabbits from the results of hyperthyroidism and acute hemolytic staphylococcus infection ($\times 150$).

two plus, three plus, or four plus. Four plus changes of an acute nature are illustrated in Figure 3.

Evidence of acute pathologic changes of significant proportions was seen in the liver in three of the eight cases. In two instances, the structural alterations consisted of marked focal necrosis and fatty degeneration. In A-16151 and A-12365, the acute changes were complicated by moderate passive congestion. In addition to the acute changes, Case A-16151 showed well-marked periportal scarring and polymorphonuclear and lymphocytic cellular infiltration. The areas of necrosis were focal in character, as shown in Figure 3,

TABLE III
DATA ON HUMAN CASES OF HYPERTHYROIDISM

Case No	Age	Sex	Color	Duration of Toxicity	B M R	Clinical Signs of Liver Damage	Treatment		Interval between Operation and Death	Grade of Chronic Liver Lesions	Grade of Acute Liver Lesions	Other Path. Changes
							with Iodine Diet and Sedation	Operation				
91064	58	F	W	9 mos	+31	0	Yes	Subtotal thyroidectomy	Avertin-ether	Crisis	9.5 hrs	+++ 0
98079	52	F	W	8 yrs	+44	0	Yes	Subtotal thyroidectomy	Avertin-ether	Crisis	6.2 hrs	+++ 0
A-11491	30	F	W	4 yrs	+48	0	Yes	Subtotal thyroidectomy	Avertin-ether	Crisis	17 hrs	0 Passive congestion of lungs and spleen
A-48640	57	F	W	6 mos	+58	0	Yes	Subtotal thyroidectomy	Cyclopropine	Crisis	21 hrs	0 0
61870	60	F	C	6 mos	+45	0	Yes	Subtotal thyroidectomy	Avertin-ether	0	15 days	0 Pulmonary embolus
59703	58	F	W	6 mos	+25	0	Yes	Subtotal thyroidectomy	Avertin-ether	Crisis	40 hrs	0 0
A-16151	19	F	W	2 yrs	+43	Jaundice Bilirubin 6.6 mg %	Yes	Daily temp to 41° C yellow atrophy 13 days after adm—in crisis	Clinical impression was acute congestive failure 8th day	+++	Passive congestion ++++	Pneumonia congestion of lungs and spleen Mediastinitis
A-12365	63	F	W	2 yrs	+72	Jaundice Bilirubin 7.2 mg %	Yes	Congestive failure on admission day Pneumonia 2 days after adm after adm—in crisis	Temp to 38° C each Dec 11 days	++	Passive congestion ++++	Pneumonia congestion of lungs and spleen

and could be separated from the slight changes resulting from passive congestion. The third case was a patient apparently well prepared for operation, and without clinical evidence of cardiac failure, however, marked passive congestion was present, even though death occurred only nine and one-half hours after operation. The liver here showed very extensive central fatty change, associated probably with the presence of passive congestion. The acute changes in the remaining five cases were insignificant.

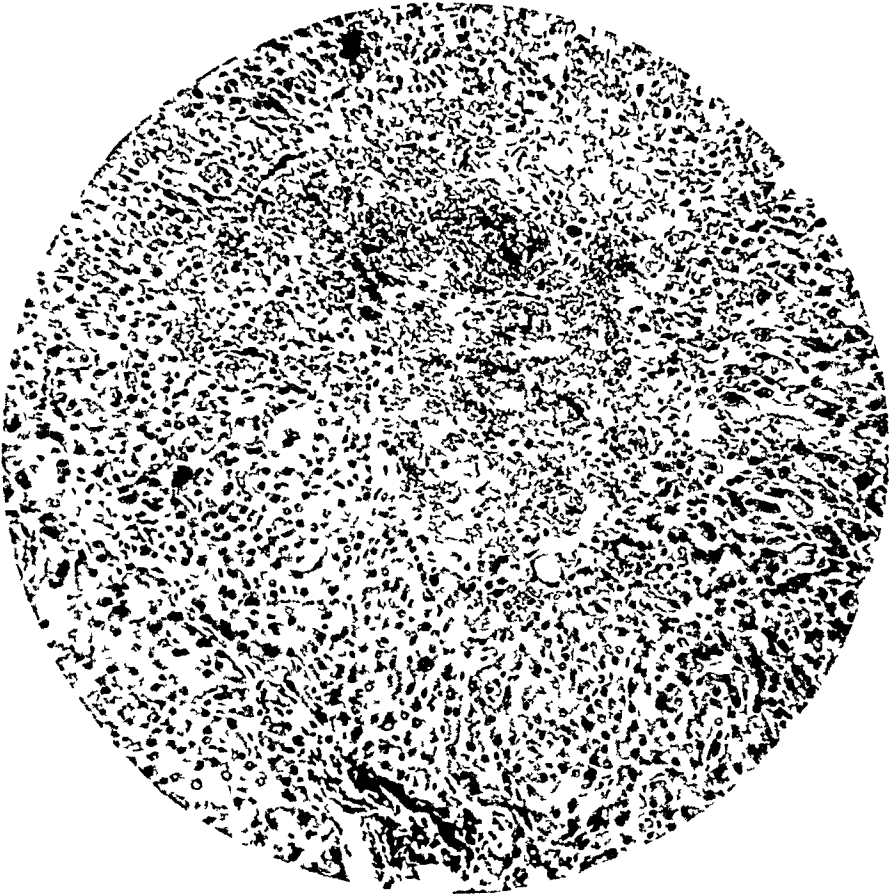


FIG. 3.—Autopsy Case A 16151. Photomicrograph of human liver showing central necrosis in a patient dying from hyperthyroidism and acute infection ($\times 150$).

The chronic lesions consisted of periportal scarring similar to that which has been described by other observers^{3, 4, 5}. Four of the eight cases showed chronic changes of this nature in significant extent while in four the damage was slight or absent. In one case of the latter four, hyperthyroidism had been of two years' duration and in the other three of only six months' duration. This seems to be significant, and a similar relationship of the duration of the toxicity with the degree of chronic change has been noted by Beaver and Pemberton.⁴

DISCUSSION —From the clinical and experimental data outlined, it is evident that uncomplicated hyperthyroidism severe enough to produce death results in no marked change in the liver structure. On the other hand, if in addition to this severe state of hyperthyroidism infection or a tissue necrosis is added, changes in the liver occur. From the previously reported experiments in which the Shope papilloma was used the question was raised of the significance of the various factors in the tumor that might in combination with hyperthyroidism result in necrosis of the liver. The factor or factors could be either the new growth *per se*, tissue necrosis, bacteria, or bacterial products. The experiments outlined in this paper show that infection alone will cause necrosis of the liver in the presence of hyperthyroidism.

There are numerous reports in the literature of pathologic changes in the liver in man as a result of thyrotoxicosis. In the majority of the cases no acute changes were noted. Weller³ did not observe any significant acute hepatic changes in a large series of cases, and it was his opinion that the slight acute alterations present were not related to the hyperthyroidism. However, Beaver and Pemberton⁴ did note a few cases of acute changes, evidently of a more severe degree but they did not attempt to explain this on the basis of combination or summation of hyperthyroidism and other factors.

No definite conclusions can be drawn from the small group of human cases here presented to prove the necessity of a factor other than hyperthyroidism in the production of liver changes, nor is information available in the literature, since the cases which have been reported were not studied from this viewpoint. However, several interesting suggestions are evident. In the two cases in which acute necrosis was seen, extensive infectious processes were present in addition to hyperthyroidism. Dependence of the liver changes on the simultaneous action of both infection and hyperthyroidism is a definite possibility. In the six cases undergoing operation, anesthetics were administered, and a possible influence of cyclopropane or avertin, especially the latter, must be considered. It was apparent from these cases, however, that changes did not accompany the use of either anesthetic. Though the anesthetics may actually be toxic to the liver in the presence of hyperthyroidism, several explanations of their lack of action in these cases are possible. In those patients with marked hyperthyroid reactions death may have occurred too quickly for the cellular changes to become evident, and had the crisis gone on for a long enough time, changes may have occurred. A second and most likely possibility was that the decrease in the severity of the hyperthyroidism by the influence of iodine, rest, and sedation as well as the liver-protective action of sufficient dietary intake was such that the summation of the action of anesthetics and hyperthyroidism was not sufficient to induce liver necrosis.

The thyroid crisis, or storm, is thought by some^{9, 10} to be the result of hepatic insufficiency. On the other hand, other observers separate the severe acute hyperthyroid reactions from the manifestations of liver insufficiency. Maddock, Pedersen, and Collier¹¹ suggested from a study of liver function and

blood chemistry in the thyroid crisis, that impaired liver function and the acute hyperthyroid reaction could both be the result of a third factor Crile¹² found liver failure occurring usually in the second or third postoperative day when the postoperative reaction is subsiding. The case of hyperthyroidism with acute yellow atrophy reported by Kerr and Rusk¹³ was interesting, in that the patient had only a moderately severe postoperative reaction, but on the 11th postoperative day became worse, on the 13th postoperative day developed jaundice, and on the 15th day after operation died, without the high temperature and pulse seen in acute hyperthyroid reactions. In addition to this clinical evidence extremely severe experimental hyperthyroidism alone, producing death in seven to ten days, was not sufficient to cause liver change. From the small number of cases presented in this article, it appears that the acute postoperative hyperthyroid reactions in patients well-prepared preoperatively are not associated with significant acute liver changes, and this is further confirmed by the low incidence of severe acute changes reported by other authors. Thus, there exists experimental and clinical evidence that the acute hyperthyroid reactions increase liver susceptibility to injury by other agents, rather than the liver failure resulting in the crisis. This seems to stress further the importance of therapeutic measures directed toward the protection of the liver from injury, not as formerly thought, as prophylaxis against an acute hyperthyroid reaction, but as a means of protecting the liver, if the acute hyperthyroid reaction develops.

As the reported experiments all deal with acute hyperthyroid reactions, no observations are available at present concerning the pathogenesis of the chronic changes observed in man. There would appear to be ample evidence from other reports that long-standing hyperthyroidism in man does produce, in a majority of cases, some chronic alteration of the liver structure. A similar change was seen in four of the eight cases reviewed. When one considers that hyperthyroidism is a disease of exacerbations and remissions and the high incidence of upper respiratory infection, a possible explanation of chronic changes in the liver resulting from the combined influence of these two factors is at once apparent.

The pathogenesis of this change in the liver seen with combination of hyperthyroidism and infection has been discussed in a previous paper.⁸ The most logical explanation seems to be exhaustion of the liver cells by the continued severe hyperthyroidism to such a degree that toxic products, that under normal metabolic activity have no effect on the liver, now result in cellular necrosis.

CONCLUSIONS

1. Uncomplicated experimental and human hyperthyroidism does not result in necrosis of the liver.
2. The combination of infection with either experimental or human hyperthyroidism results in necrosis of the liver.
3. Chronic lesions are present in long-standing cases of hyperthyroidism.

- 4 The relationship of the liver lesions and thyroid crisis is discussed
- 5 The pathogenesis of the acute changes is suggested

BIBLIOGRAPHY

- ¹ Youmans, J B, and Warfield, L M Liver Injury in Thyrotoxicosis as Evidenced by Decreased Functional Efficiency Arch Int Med, 37, 1-17, January, 1926
- ² Bartels, E C Liver Function in Hyperthyroidism as Determined by Hippuric Acid Test Ann Int Med, 12, 652-674, November, 1938
- ³ Weller, C V Hepatic Pathology in Exophthalmic Goiter Ann Int Med, 7, 543-560, November, 1933
- ⁴ Beaver, D C, and Pemberton, J de J The Pathologic Anatomy of the Liver in Exophthalmic Goiter Ann Int Med, 7, 687-708, December, 1933
- ⁵ Cameron, G R, and Karunaratne, W A E Liver Changes in Exophthalmic Goiter Jour Path and Bact, 41, 267-282, September, 1935
- ⁶ Means, J H Thyroid and Its Disease J B Lippincott Co, Philadelphia, 1937, p 319
- ⁷ Haban, G Leberneränderungen bei experimentellem Hyperthyroidismus Beitr path Anat u allg Path, 95, 579-589 September 1935
- ⁸ Sealy W C The Induction of Liver Necrosis in Rabbits by the Combination of Experimental Hyperthyroidism and Shope Papilloma, ANNALS OF SURGERY, 113, 572-578, April, 1941
- ⁹ Lahey, Frank Reduction of Mortality in Hyperthyroidism New England Jour Med, 213, 475-479, September 5, 1935
- ¹⁰ Boyce, F F, and McFetridge, E M Studies of Hepatic Function by Quick Hippuric Acid Test Thyroid Disease Arch Surg 37, 427-442, September, 1938
- ¹¹ Maddock, W G, Collier, F A, and Pedersen, S Studies of the Blood Chemistry in Thyroid Crisis J A M A, 109, 2130-2135, December, 1937
- ¹² Crile, G, Jr Liver Failure in Postoperative Delirium in Patients with Hyperthyroidism West Jour of Surg, 48, 438-444, July, 1940
- ¹³ Kerr, W J and Rusk, G Y Acute Yellow Atrophy and Hyperthyroidism Med Clin N Amer, 6, 445-459, September, 1922

CRUVEILHIER-BAUMGARTEN SYNDROME (SPLENOMEGALY, PORTAL HYPERTENSION AND PATENT UMBILICAL VEIN)

CASE REPORT

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ASIDE from those conditions, such as Laennec's cirrhosis, Banti's disease, portal thrombosis, *etc*, commonly thought of as causes of splenomegaly, with evidence of disturbed portal circulation, there is a rarer disorder which is accompanied by a somewhat similar clinical picture. This is the syndrome described first by Cruveilhier, in 1852, and later by Baumgarten, in 1908, and characterized by portal hypertension with splenomegaly and evidence of excessively prominent umbilical circulation, *i e*, visible abdominal veins and a venous thrill and murmur.

Although this syndrome has been recognized in the European literature for a number of decades, the first discussion to appear in English was that of Armstrong, *et al*¹ (1942), who believe that any patient who presents the picture described by Cruveilhier and Baumgarten merits the diagnosis of Cruveilhier-Baumgarten syndrome, and those cases which show at autopsy a patent umbilical vein with an associated atrophic liver with little or no fibrosis would be considered as instances of Cruveilhier-Baumgarten disease. Armstrong, and his coworkers, were able to find 52 previously reported cases, and to these they added three patients whom they had studied.

We have recently had the opportunity to observe a patient with this unusual disorder, and the purpose of this communication is to add to the literature another instance of this syndrome. The clinical findings as well as the findings at the time of operation are presented.

Case Report—V L J, male, age 20, was admitted to the Medical Service, March 3, 1942, with a chief complaint of a diarrhea, with seven to nine watery stools daily for eight weeks. There had been no bloody, tarry or acholic stools. There were no significant findings in the family, marital or past histories, except that one of his younger brothers, age seven, also has a splenomegaly of unexplained etiology.

Physical Examination—The patient was a well-developed and well-nourished boy, who appeared to be in good health. There were several small, discrete, nontender, firm inguinal lymph nodes. The abdominal veins were minimally dilated. The abdomen was asymmetrically prominent, with a fullness in the left hypochondrium. Filling the entire left side of the abdomen was a large smooth, nontender mass which was readily movable and had an easily palpable notch just opposite the umbilicus. A continuous thrill, which disappeared on light pressure, was felt four centimeters to the right of the umbilicus. Auscultation over this area revealed a constant, roaring hum without systolic accentuation which could be traced laterally and superiorly toward the liver. This, too, could be abolished by light pressure.

Laboratory Data Hemoglobin 12.2 grams (15.5 grams = 100%), erythrocytes 4,500,000 per cc, and there was a constant leukopenia averaging 3,000 leukocytes per

cc, and varying from 2,600 to 3,800. A typical differential leukocyte count showed segmented polymorphonuclears 50%, nonsegmented polymorphonuclears 8%, eosinophils 3%, small lymphocytes 32%, large lymphocytes 3%, monocytes 4%. Of the three differential counts made prior to operation, one showed an eosinophilia of 6%, and another showed 3% eosinophils. Repeated blood smears were negative for malarial parasites. Liver function studies (icteric index, galactose tolerance and bromsulphalein) were all within normal limits. One hour following subcutaneous injection of 0.5 cc of 1:1000 epinephrine the leukocyte count was 3,920, and the erythrocyte count was 4,875,000, as compared with 2,850 and 4,850,000, respectively, immediately before the injection. Bleeding and coagulation times were not increased. Fragility test. Hemolysis started at a concentration of 0.38% NaCl and was complete at 28% as compared with the control of 0.40% and 0.38%. Platelet count was normal. Biopsy of an inguinal lymph node revealed chronic lymphadenitis. The sternal bone marrow was normal. No varices were demonstrated in the barium filled esophagus. A film of the abdomen after the intravenous injection of Thorotrast showed no defects in the splenic shadow and the liver shadow was not enlarged. Repeated stool examinations were negative for blood, parasites and amoebae. Proctoscopic examination was negative except for a slightly edematous rectal mucosa. Repeated urinalyses were negative.

On March 23, 1942 the patient was transferred to the Surgical Service and a celiotomy was performed. In the abdominal wall many dilated veins were encountered, some of these were a half centimeter in diameter, and had to be clamped and cut. Upon opening the abdominal cavity a mass of cirroid veins, some one centimeter in diameter, were seen lying directly underneath the umbilicus. The umbilical vein was dilated and tortuous. The spleen filled the entire left half of the abdomen, and had a firm, fibrotic appearance, with a definite bluish cast. Palpation of the spleen revealed no adhesions to the diaphragm or surrounding structures. The liver was questionably smaller than normal and had a coarse granular appearance, but was not typically hobnail. The portal system was not visualized, but the vessels were normal to palpation. The splenic pedicle was found to contain many dilated vessels and, following the injection of three cubic centimeters of 1:1000 adrenalin directly into the spleen, these vessels were individually ligated and the spleen delivered without difficulty. An accessory spleen, approximately 4 x 2.5 cm in size, was removed. A biopsy of the liver was then taken, and the abdominal wall anatomically approximated.

The patient withstood the procedure well, and his postoperative course was satisfactory. There was a rather marked leukocytosis of 28,700 immediately postoperatively, which subsequently became stabilized at about 9,000 leukocytes per cc. Two of the three differential blood counts made within a week after operation showed an eosinophilia of 1% and 3%, respectively, while three counts made during his final 11 days in the hospital did not show any eosinophils. The patient was discharged on the eighteenth postoperative day, and at that time his hemoglobin was 14.8 grams, erythrocytes 5,200,000, leukocytes 9,400 per cc, platelet count normal and a normal blood differential count. The abdominal venous thrill and murmur were still present at the time of discharge.

Pathologic Examination—Gross. Dr. Robert P. Morehead: "The spleen weighs 1700 grams. The outer surface is smooth. The cut surface is reddish-brown and beefy in appearance. The fibrous tissue of the organ is not increased grossly. A specimen of liver, which measures approximately 1 x 0.8 x 0.6 cm, is included. *Microscopic*. Sections of the spleen show a small amount of diffuse fibrosis and the trabeculae are larger than normal. The blood spaces in the spleen are prominent and scattered throughout the structure are numerous eosinophils and a few neutrophils. Sections through the liver show periportal fibrosis and mononuclear and eosinophilic infiltration. In certain areas active fibrosis is seen beneath the liver capsule, and here one sees bile duct proliferation. There appears to be some thickening of the central and

interlobular veins In certain instances there is some hyalinization of the thickened vascular wall"

Subsequent Course—The patient was last seen three months after discharge At that time he was beginning to resume his former activities Physical examination was not remarkable except for the venous thrill and murmur previously described

Comment Not only does this case conform to the criteria stated above but it is, so far as we have been able to discover, the first instance of Cruveilhier-Baumgarten syndrome in which splenectomy and liver biopsy have been performed The splenectomy was not undertaken in an attempt to alter the pathologic process, but because it was our opinion that the possibility of traumatic rupture of the spleen in a young farm boy was very real It will be of considerable interest to see if the life of this patient is prolonged over that of those previously reported Most of the reported cases have died of portal decompensation or of hepatic insufficiency, and the average age at death was 30.4 years in those instances where the umbilical vein was patent, contrasted to an average of 38.2 years for the entire unselected group The exact cause of death was determined in only one-third of the cases and, of these, hematemesis was the most frequent terminal episode

The presence of an eosinophilia of 6% in one of the three preoperative differential blood counts, and 3% eosinophils in another, in the absence of intestinal parasites, and the common causes of eosinophilia, is an interesting finding in this case Differential blood counts postoperatively were within normal limits (two of six counts showing 1% and 3% eosinophils) Differential counts are recorded in only 10.8% of the cases reviewed by Armstrong, *et al*, and there is no mention of an eosinophilia However, in view of the numerous eosinophils found in this patient in the liver and spleen, it would seem that eosinophils should be looked for in future cases

A constant leukopenia, on the other hand, has been frequently observed in this condition, and it was a consistent and striking finding in our patient In the previously reported cases, in which a leukocyte count was recorded (15), a leukopenia was present in 46.6%, and three other cases had a leukocyte count of less than 6,000 In our patient the postoperative leukocytosis of 28,700 was expected However, following splenectomy the leukocyte count became stabilized at a normal figure, and has remained between 7,500 and 9,500 for three months We believe that a persistent leukopenia of below 4,000 is an important addition to the criteria for the diagnosis of the Cruveilhier-Baumgarten syndrome

While the differentiation of this syndrome from the more common causes of splenomegaly combined with signs of disturbed portal circulation, such as Laennec's cirrhosis Banti's disease, *etc*, is important, it is perhaps more difficult to be sure that the patient does not have either portal thrombosis or that rare condition—a primary splenic tumor It was suggested that the response of the blood leukocyte and erythrocyte counts to the injection of adrenalin might be of value in determining the diagnosis of splenic thrombosis This procedure consists of the subcutaneous injection of 0.5 cc of 1:1000 adrenalin and recording the leukocyte and erythrocyte counts im-

mediately before and one hour following the injection. In our patient this procedure produced results which were not conclusive enough to infer patency of the splenic vein or to postulate a thrombosis. The procedure was, therefore, of no value in demonstrating patency of the portal circulation. We believe that visualization of the spleen by means of intravenous thorotrast is the most valuable procedure to rule out a primary splenic neoplasm. There was no evidence of such disease in our case.

The findings in the present case suggest that Armstrong, *et al*, are correct in their assumption that the clinical picture in this syndrome is probably dependent upon portal hypertension associated with patency of the umbilical vein and consequent shunting of the blood away from the liver into the systemic circulation. This particular anatomic arrangement can be produced by a variety of etiologic factors, as is pointed out in the cases summarized by Armstrong. Although in those cases there was no reference to the occurrence of this disorder in more than one member of a family, it will be of particular interest to follow our patient's younger brother regarding the etiology of his splenomegaly.

We believe that any patient who shows splenomegaly without hepatomegaly, distended abdominal veins, an abdominal venous thrill and murmur, a persistent leukopenia and an eosinophilia, merits the diagnosis of Cruveilhier-Baumgarten disease. We agree with Armstrong, *et al*, that the presence of the venous thrill and murmur is the most important feature from the standpoint of diagnosis, but we also feel that leukopenia and, if present, eosinophilia, are important findings in this unusual disorder.

SUMMARY

A case of Cruveilhier-Baumgarten syndrome is being reported. This is the 56th case of this condition to be described, and the first in which splenectomy and liver biopsy have been performed.

REFERENCE

- ¹ Armstrong, E. L., Adams, W. L., Tragerman, L. J., and Townsend, E. W. *Ann Int Med*, 16, 113, 1942.

DUODENAL TUMOR OF UNUSUAL CHARACTER

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AND

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THIS PAPER has been prepared for the purpose of recording a case which should be of particular interest to the internist, pathologist, radiologist, and surgeon, for the following reasons

1 It demonstrated an unusual cause for the presence of vague epigastric distress associated with diarrhea, occult blood in the stool, anemia, and loss of weight

2 The pathologico-anatomic lesion is of interest, and its origin provocative of discussion

3 The roentgenogram was deceptive, and of great interest

4 The case can be added to that increasing, but relatively small, number in which a malignancy of the ampullary portion of the duodenum and adjacent pancreas has been successfully removed So far as can be determined, it is the only myosarcoma in the more than 125 cases reported in that series

Case Report—The patient, a married woman, age 61, was first seen by one of us (A M F), August 9, 1941, being referred by Dr Wilbur Skillman At this time her complaint was anemia for five years, and diarrhea for three months The family history was not important, her father and mother having both died in their 80's The patient had had a bad attack of rheumatic fever at 19, with no return of joint pains until an attack of arthritis four years ago, which involved all her joints, with swelling and pain These symptoms finally cleared up after a tonsillectomy three and one-half years ago The present illness dates back five years, at which time she had symptoms of weakness, sore tongue, numbness of the hands and feet, and constipation A diagnosis of pernicious anemia was made, and she was given 12 injections of liver extract intramuscularly, and liver and liver extract by mouth An hemorrhoidectomy was performed at this time because of bleeding Four and one-half years ago a panhysterectomy was performed because of a diagnosis of myomata, one of which, however, proved, microscopically, to be a myosarcoma (Fig 7) Her recovery from this operation was uncomplicated and except for the arthritis which was mentioned earlier, she remained well until May, 1941 This was three months before her examination, and she then developed rather marked diarrhea which continued without interruption The stools varied in number from 4 to 8 in 24 hours They were most apt to come early in the morning starting at 3 or 4 o'clock, and again once or twice before breakfast The stools were always bulky, but never watery At first they had a yellowish, curd-like character, later becoming grayish and at times foamy They were always extremely foul-smelling, but never contained any blood She had not suffered any severe abdominal pains but complained of some soreness over the left lower quadrant of the abdomen of a colicky character, and occasional discomfort in the epigastric region There was no nausea or vomiting Soreness of the tongue was not a symptom during this time, but she did notice that her gums were sore in places She occasionally noticed numbness of the hands and to a less extent of the feet and had some unsteadiness when on her feet, which she interpreted as being due to weakness

Physical Examination—Temperature 99.4°F, pulse 96, blood pressure 108/65. She was much underweight, rather pale, and looked quite ill. The skin was smooth and soft, there was no icterus and no skin lesions, but some large brown freckles over the forearms and backs of the hands. The eyes were deep-set and the lids very dark. Dental plates were worn and there was no abnormality to be made out of the gums, mucous membranes of the mouth or of the tongue, which was neither smooth nor red. There was no adenopathy. The lungs were entirely clear, and the heart was normal except for the presence of numerous extrasystoles and a soft systolic murmur at the apex. Abdominal examination revealed nothing except a little tenderness in the left lower quadrant and over the upper part of the abdomen, bilaterally, with a definite sensation of resistance in the epigastrium. The liver edge was just palpable, it felt quite normal. The spleen was not felt. The fingernails were quite soft and thin. There was some swelling of the right leg associated with rather extensive varicose veins. The neurologic examination revealed only some generalized muscle weakness, sluggish knee jerks and some uncertainty of gait, apparently due to weakness; there was no spasticity. The Romberg test was negative, and vibratory sense normal over hands, legs and spine.

Laboratory Data—The urine was normal except for a trace of albumin. The hemoglobin was 77 per cent (Sahli), RBC, 3,970,000, WBC 6,200. Differential: Polys 64 per cent, L 22 per cent, Mono 14 per cent, the red blood cells were normal in size and shape, no anisocytosis nor poikilocytosis, platelets were rather scarce. The smear did not in the least resemble that of pernicious anemia.

The preliminary impression was that the patient presented a history and a picture suggesting nontropical sprue. It was felt that this would fit in with the former diagnosis of pernicious anemia, which evidently was not characteristic and did not respond well to liver therapy. It was noted, however, that if she had had sprue at that time it also should have shown a better response to liver. The second most likely diagnosis was thought to be carcinoma involving some part of the gastrointestinal tract.

Stool specimens were examined and found to be bulky, semiformed, and to contain much undigested food. The first specimens did not show a definite increase in fat, as far as could be determined by gross and microscopic examination. The benzidine test showed a strong reaction for occult blood and the guaiac test showed a weak positive. In another examination following restriction of meat the benzidine test was again strongly positive.

Gastric analysis following an Ewald test meal revealed no free acid, and 10 per cent of combined acid.

Roentgenologic examination of the gastro-intestinal tract, 8/11/41, by Doctors Waters and Firor was reported as follows:



FIG. 1—Roentgenogram of stomach and duodenum after the ingestion of barium showing the filling defect in the duodenum caused by the tumor.

"The stomach and duodenal cap are normal. A defect in the duodenum is observed extending from the distal portion of the cap into the descending portion of the duodenum approximately to the region of the ampulla of Vater. This defect is sharply outlined, especially in its lower portion, and appears intrinsic rather than as the result of pressure from some extraduodenal mass. The barium mixture passes around the defect in a thin stream and discloses a normal mucosal pattern along the upper and lateral margin of the duodenum (Fig 1). *Röntgenologic Diagnosis*. The findings indicate a neoplasm in the duodenum the nature of which is indefinite. The vast majority of reported benign neoplasms of the duodenum have occurred in the duodenal cap, whereas the rare malignant lesions have been in the region occupied by this mass, but the sharply demarcated character of the defect in this case strongly favors benignity."



FIG 2—Drawing showing the site of the tumor and the extent of the resection, as well as the location of the common duct

Some improvement in her diarrhea followed the administration of dilute hydrochloric acid, a low residue, low carbohydrate diet, but otherwise she did not improve. She was bothered a good deal with pain in the epigastrium and became increasingly weak and pale. It was then felt that the lesion in the duodenum might well be a malignant one and that it might be responsible for many of her symptoms. On September 17, 1941, an exploratory operation was performed by one of us (R.T.S.), at the Union Memorial Hospital in Baltimore.

Preoperative Diagnosis. Benign polyp of the ampullary portion of the duodenum.

Operation—Under nitrous oxide, followed by drop-ether anesthesia, the abdomen was opened through an upper right rectus incision. On exploration, an intrinsic mass the size and shape of a lemon was felt within the descending portion of the duodenum, apparently attached to the posterior duodenal wall but not elsewhere. There were no

other masses seen or felt in the liver or other portions of the peritoneal cavity. The gallbladder appeared normal. The anterior wall of the duodenum opposite the tumor was opened longitudinally in order to inspect the lesion by direct vision. It was then seen to be an oblong, reddish, firm, polypoid mass attached to the posterior wall of the duodenum throughout the length of the tumor by an indurated, sessile base extending from about one-half inch below the pylorus to the ampulla of Vater. Its location made preservation of the latter impossible if the former was to be removed. Resection of that portion of the duodenum containing the tumor (Figs 2 and 3) was decided upon. Accordingly, the duodenum was mobilized medially by incising its lateral peritoneal attachments.



FIG 3—Drawing showing the appearance after completion of the resection of the ampullary portion of the duodenum and part of the head of the pancreas, with a Billroth I gastroduodenostomy, ligation of the common duct and cholecystogastrostomy.

The duodenum was then transected between Stone anastomosis clamps at a point one inch below the ampulla of Vater, which was at the lower border of the tumor. Both cut ends were carbolyzed. The common duct was positively identified by withdrawing bile from its lumen through a small hypodermic needle. It was then isolated and cut across about one inch from its entrance into the duodenal wall. Its cut proximal end was ligated with No. 1 chromic catgut reinforced by a second ligature of medium black silk. The stomach was sectioned one inch above the pylorus. This left the intervening segment of duodenum containing the tumor and ampulla attached to the pancreas along its posterior wall. A small portion of the head of the pancreas was transected by sharp dissection at a sufficient distance to have a seemingly safe margin at the base of

the tumor The duodenum with its attached pancreas was then removed *en masse* The cut surface of the pancreas was closed with interrupted silk sutures

The unusual mobility of the remaining distal segment of duodenum made it possible to perform a Billroth I, end-to-end gastroduodenostomy, which was accomplished by means of an inner continuous suture of the mucosal surfaces with No 0 plain catgut and a serosal row of interrupted fine silk sutures

Because the common duct could be implanted into the intestinal tract only under marked tension, it was considered preferable to provide a pathway for bile by means of a cholecystogastrostomy which could be done without any tension whatsoever This was accomplished in the usual way with two layers of sutures The omentum was placed over both suture lines and the abdominal wound closed in layers using catgut for the deeper sutures, silk for the skin and through and through stay sutures of braided silk One Penrose drain was placed down to, but not into, the peritoneum and brought out at the lower end of the incision

During the procedure the patient received a transfusion of 500 cc of citrated blood plus 1000 cc of 5 per cent glucose intravenously

The operation required two and one-half hours, and the patient returned to her room in good condition, with pulse 126, blood pressure 138/90

The postoperative period was a stormy one, being complicated by bilateral pulmonary consolidation, for which she received sulfathiazole, phlebitis of the great saphenous vein of the right leg, transitory jaundice, and generalized edema This latter was thought to be mainly due to a very low serum protein level, which on September 20th, was 3.5 grams per cent, and on September 23rd 4.1 grams per cent Other laboratory studies were reported as follows Stool examination, on October 9th, showed much gross fat which was stained with Sudan III A specimen examined on October 16th showed little fat Blood chemical studies on September 20th were N P N 29, blood chlorides 522, blood calcium 8.4, and blood phosphorous 1.1 On September 23rd, N P N 33, blood chlorides 517, CO₂ combining power 54 volumes per cent, and on October 11th, blood calcium 9.2 milligrams per cent and blood phosphorous were 4 milligrams per cent

On the 13th postoperative day the temperature which had been falling began to rise in daily peaks, and on the 16th postoperative day signs of free fluid in the abdomen appeared and the patient's condition became critical That evening, under local anesthesia in her room, an opening was made in the healed incision and a clamp inserted into the peritoneal cavity There was an immediate gush of a large quantity (several hundred cubic centimeters) of grayish fluid containing particles of necrotic material A Penrose drain was inserted, and the patient's condition immediately improved and continued to do so until her discharge from the hospital on her 37th postoperative day At the time of discharge she was ambulatory and consuming a low fat diet, but one high in carbohydrate and protein, with liver two or three times a week, and additional vitamins The wound had healed except for a small sinus at its lower border which exuded a small amount of fluid This healed two weeks later and has remained healed

On November 26th, she was found to be still improving and had gained three or four pounds She was still bothered by cramp-like abdominal pains, gas and eructation and was having an average of two stools a day, which were quite light in color but formed or semiformed On January 5, 1942, she looked definitely better but the diarrhea, which has never entirely cleared up, was now worse again, and in spite of a very good appetite, she was not gaining weight The diarrhea was never watery, but the stools were bulky and at times foamy in character Her hemoglobin was then 90 per cent It was felt that these symptoms were due mainly to lack of external secretion of the pancreas and pancreatin was then administered in doses of 0.9 Gm three times daily, and is being continued

She was next seen February 26, 1942, when she reported that she was feeling

DUODENAL TUMOR

a great deal better and gained four more pounds. Her diarrhea was much less marked but she still had two or three stools a day, which were quite bulky. She was advised to continue the same regimen of treatment.

On March 18, 1942, she reported great symptomatic improvement. She was having almost no symptoms and had gained weight and strength. Her color was much better and her general appearance was one of quite good health. The following blood chemical studies were made, the results of which are all well within normal limits. Blood



FIG 4—Photograph of duodenal segment. Tumor—measures $3\frac{1}{2} \times 2\frac{1}{2} \times 1$ inches. Covered by mucosa and extending into muscular wall. Ampulla is situated at corner margin of mass.

calcium 9.5 mg per cent, blood phosphorous 3.9 mg per cent, total proteins 7.06 per cent, and fasting blood sugar 81 mg per cent. The stool at this time was semiformal, yellowish-brown in color, and contained no gross fat. There was no occult blood by the guaiac test.

The patient was progressing quite satisfactorily until May 30, 1942. At this time, the stools were almost normal but she was having pain in the cervical spine. She had lost some weight and the hemoglobin had dropped to 75%. On June 9, 1942, she had much worse pain in the cervical spine and had developed flaccid paralysis of

the left arm and some weakness of the left leg and of the face on that side. At this time, she looked a great deal worse and it seemed obvious that she had metastatic carcinoma involving the cervical spine and brain. From that time on she went downhill rapidly with progressive increase in paralysis, coma, and death on June 25, 1942. An autopsy was not done but there can be no doubt that metastases from her original carcinoma were the cause of death.

Pathologic Examination—Gross Dr W C Merkel The specimen consists of a

FIG 5

FIG 7

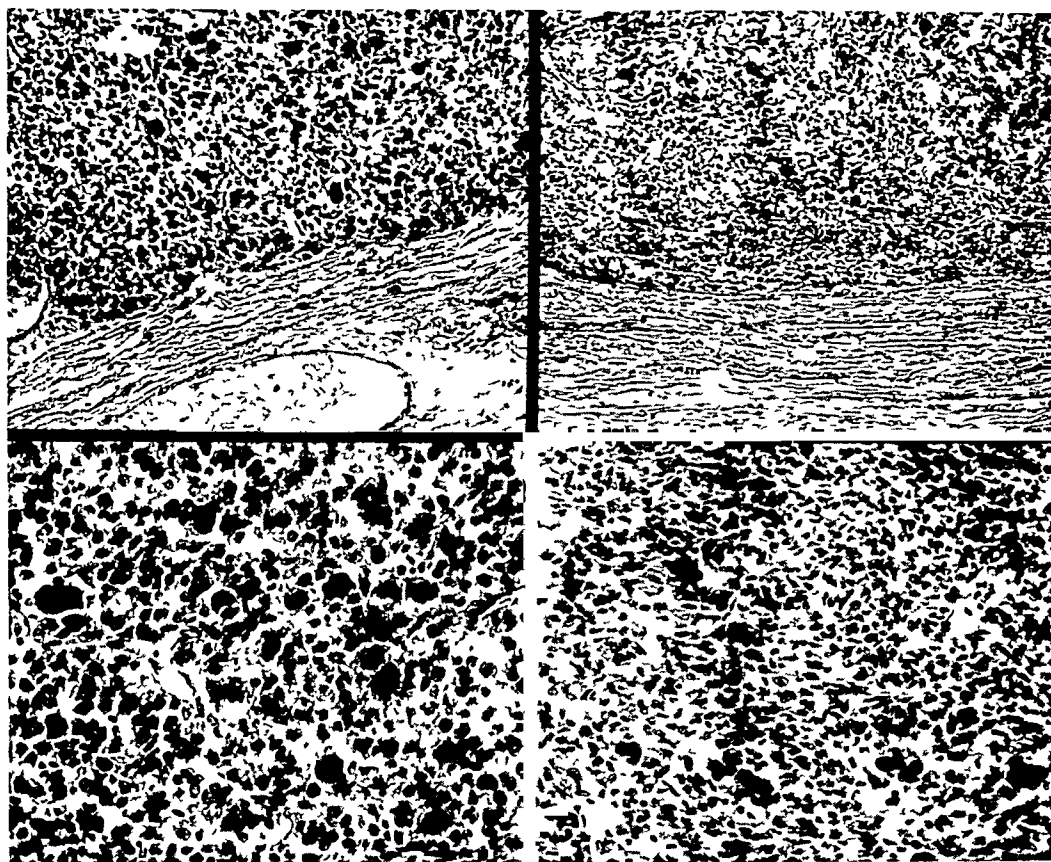


FIG 6

FIG 8

FIG 5—No 21777 Photomicrograph of section through duodenal tumor. Note regular muscular border. Similar multinucleated giant cells and lack of cell patterns. (×100)

FIG 6—No 21777 Higher magnification of section from duodenal tumor removed October, 1941. Note large multinucleated giant cells, loose vascular stroma, and pleomorphic cell morphology. (×200)

FIG 7—No 13555 Photomicrograph of tumor removed (3.3.37). Uterine fibromyoma, with encapsulation. Note multinucleated cells, vascular spaces, and pleomorphic cell morphology. The uterine wall forms a straight line of demarcation. (×100)

FIG 8—No 13555 Higher magnification of section taken from uterine myoma (3.3.37). (×200)

segment of the duodenum, five inches in length, containing an oval-shaped, sessile polyp on the pancreatic side of the duodenal wall. The polyp measured $3\frac{1}{2}$ inches in the long diameter and $2\frac{1}{2}$ inches in the transverse diameter, and its depth was $1\frac{1}{2}$ inches. The surface is lobular, smooth and gives the impression of a thin layer of mucosa (Fig 4). The cut surface is of a grayish white color forming no pattern and giving the impression of being glandular tissue. The growth infiltrates the muscular wall but the serosa is uninterrupted. Microscopically, the sections form a very sharp line of demarcation. It appears as though the muscle were displaced by the growth.

The tumor is moderately vascular. There are many well-formed blood vessels which would indicate that these have not existed prior to the tumor invasion. There is marked variation in the morphology and size of the cells. Multinucleated, huge giant cells are numerous. The other cells which predominate have oval shaped nuclei. The cytoplasm is flocculent. Mitotic nuclei are numerous. There is no leukocytic infiltration, nor is there any stroma formed by the tumor tissue which would give support. There is a total absence of any cell pattern. There are areas of hemorrhage. The tissue adjacent in some areas is pancreas while most of the surrounding structures are muscle from the wall of the duodenum. Occasional lymphatics contain tumor cells, and the lymphoid stroma encountered is not infiltrated, nor does it show any evidence of resemblance to tumor cells which would probably rule out an endotheliomatous type of sarcoma. *Pathologic Diagnosis* Myosarcoma (comparing the growth with No 13555 (Figs 7 and 8) which was a myosarcoma of the uterus, removed from the same patient in 1937, indicates that this is probably metastatic).

There are several points about the above case which deserve further consideration. One of great interest is whether the tumor represents a metastasis from the original myosarcoma of the uterus, removed four years previously, or whether it is another primary tumor in a different location. Microscopically, the two lesions are identical, but the fact that the lesion occurred in the duodenum, a rare, if not unique, site for such a metastasis plus the fact that, so far as could be determined, it is solitary, is very much against the possibility of its having originated in the uterus. On the other hand, myosarcomata of the duodenum as well as multiple myosarcomata in the same patient have been reported, although a very cursory and incomplete survey of the literature has not revealed a similar distribution. Our opinion favors the view that the second lesion was primary in the duodenum.

Another point of interest is the fact that the patient suffered from a sprue-type of diarrhea previous to operation. This could be explained by pointing out that the pancreatic duct traversed the tumor before joining the common duct and, hence, pancreatic secretions may have been blocked from entrance into the intestinal lumen. Jaundice was not present as the common duct entered the duodenum just below the tumor and in a direction which escaped impingement by the lesion.

The blood chemical findings are of considerable interest. In steatorrhea, whether of pancreatic origin—as we assume this to be—or due to sprue, it is common to find a low level of serum calcium and phosphorus. These abnormal values have been shown to be due to poor absorption from the intestinal tract, as is shown by excessive fecal excretion of these substances while their urinary excretion is lowered. This decreased absorption is best explained, at least in the pancreatogenous type of steatorrhea, as being due to two factors. (1) The excess of fat in the intestinal contents holds vitamin D in solution, thereby preventing its action in promoting calcium absorption and causing more of it to be excreted in the feces, and (2) calcium forms insoluble soaps with excessive fatty acids and cannot be absorbed normally. Lowered serum proteins are also to be expected under these circumstances and may be related to an increased nitrogen excretion in the

feces, which does take place in the pancreatogenous-type of fatty diarrhea in contradistinction to the sprue-type in which it is usually within normal limits. This was pointed out by Thaysen,³ who felt that the fecal nitrogen determination was a good criterion in the differential diagnosis of steatorrhea. In our patient, it is well to remember, however, that these blood chemical studies were made several days after the operation and were certainly modified to some extent by the various factors that are known to alter their values under those conditions.

The roentgenogram (Fig 1) was also of interest as the smooth outline of the defect strongly suggested that the lesion was benign. The fact that it proved to be malignant is worth serious consideration in the interpretation of other films revealing a similar picture.

The operative attack upon these lesions was initiated by Dr W S Halstead,¹ who, in 1898, first removed a carcinoma of the ampulla of Vater by removing the duodenum, performing a Billroth-I gastroduodenostomy, and reimplanting the common and pancreatic ducts into the duodenum. At the same time he performed a cholecystostomy. His patient succumbed seven months later from a recurrence of the tumor. Since that time, other isolated reports of similar procedures have appeared in the literature and have been summarized by Hunt.¹ Recent interest has been stimulated by the writings of Whipple,^{5, 6, 7, 8} and his colleagues, who have had particular success with their modifications of the procedure, while the courage to attack this particular case was derived to some degree from the recent success with which Dr I R Trimble, of this city, performed a similar operation, which has been reported elsewhere.⁴ The articles by Whipple, Hunt and Trimble can be recommended to those interested in the subject as in these will be found a thorough history of the methods of surgical attack, the results, and a tabulation of the cases reported in the literature.

In reviewing the above articles, one or two thoughts on the technic of the operation seem worthy of mention. It was pointed out by Whipple that a large proportion of these cases develop postoperative drainage for varying lengths of time. Presumably, in most instances this has come from the cut surface of the pancreas. In our case no provision was made for the drainage of this fluid which accumulated within the tightly closed abdomen and nearly caused the death of the patient. The drainage was followed by prompt improvement and recovery. In any future similar operation it is our plan to provide such drainage at the time of operation.

Some writers emphasize the point that it is more satisfactory to reimplant the stump of the common duct into the duodenum, as contrasted with the restoration of biliary drainage by means of a cholecystogastrostomy. The latter was performed in this particular patient and, in our opinion, rightly so. The duct could have been reimplanted only under hazardous conditions of tension while the gallbladder lay readily adjacent to the stomach. It is our belief that the most satisfactory operation is the one which technically is the

easiest to perform and at the same time accomplishes the purpose for which it is planned

SUMMARY

We have presented a case of a duodenal tumor which was of particular interest for the following reasons

1 The patient had a spume-like diarrhea, associated with anemia and occult blood in the stools

2 The smooth outline in the roentgenogram suggested a benign rather than a malignant lesion

3 The tumor was a myosarcoma of the duodenum, in a patient who had had a myosarcoma of the uterus removed four years previously

4 The lesion was successfully treated by removing the ampullary portion of the duodenum with the adjacent portion of the head of the pancreas, and then performing a cholecystogastrostomy and a Billroth-I gastroduodenostomy

REFERENCES

- ¹ Hunt, Verne C Surgical Management of Carcinoma of the Ampulla of Vater and of the Periapillary Portion of the Duodenum ANNALS OF SURGERY, 114, 570-602, October, 1941
- ² Orr, Thomas G Resection of Duodenum and Head of Pancreas for Carcinoma of the Ampulla Surg Gynec & Obst 73, 240-243, August, 1941
- ³ Thaysen T E Hess Ten Cases of Idiopathic Steatorrhea Quar Jour Med, 4, 359, 1935
- ⁴ Trimble, I Ridgeway, Parsons, John W and Sherman, Claude P A One-Stage Operation for the Cure of Carcinoma of the Ampulla of Vater and the Head of the Pancreas Surg, Gynec & Obst, 73, 711-722, November, 1941
- ⁵ Whipple, Allen O Surgical Treatment of Carcinoma of the Ampullary Region and Head of the Pancreas Am Jour Surg, 40, 260-263, 1938
- ⁶ Whipple, Allen O Personal communication
- ⁷ Whipple, Allen O, and Frantz, Virginia Kneeland Adenoma of Islet Cells with Hyperinsulinism ANNALS OF SURGERY, 101, 1299-1335, 1935
- ⁸ Whipple, Allen O, Parson, William Barclay, and Mullins, Clinton R Treatment of Carcinoma of the Ampulla of Vater ANNALS OF SURGERY, 102, 763-779, 1935

VOLVULUS OF THE CECUM

REPORT OF FOUR CASES

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TORSION OF THE CECUM, usually with involvement of adjacent terminal ileum and ascending colon, is of sufficient rarity to warrant the report of single cases Bundschuh,¹ in 1913, collected reports of 110 cases, to which Wolfer, Beaton and Anson² added 194, in 1942 The importance of the lesion in the differential diagnosis of right lower quadrant pain and intestinal obstruction is emphasized by the 100 per cent mortality by conservative treatment, the relative ease with which the diagnosis is established or confirmed by roentgenologic examination, and the simplicity of the necessary surgery early in the disease

In their recent exhaustive anatomic study, Wolfer, Beaton and Anson group the extreme variations in ileocolic peritoneal fixation into six major types They stress, on the basis of the evidence in the literature, and their 125 dissections, that not only must hypofixation (persistent common mesentery, imperfect fixation) of an adequate degree be present, but that some degree of hyperfixation of ileum, cecum, or ascending colon supplies the fixed point for the rotation They note that no one specific accessory activating factor is apparent, and conclude that physiologic maladjustments (hyperperistalsis, *etc*), acting on an anatomic predisposition, provide the inciting etiologic causes Hence, variable hypofixation, many possible inciting causes, and other variations are found

Rotation may be axial, in the frontal, or in the sagittal planes, or in any two or all of these Dependent upon the disposition of the peritoneum, the twisted portion may be as little as the tip of the cecum, or as much as the entire colon

Whatever the inciting cause, there is usually sufficient early axial twist to obstruct the ascending colon The ileocecal valve permits progressive enormous dilatation of the effectively closed loop The result of this distention on the mural branches of the ileocolic vessels, the latter already compromised by tension and pressure on the trunks, is the late vascular damage so frequently described The location of the fixed point, the contour of the iliac fossa, the sacral promontory, and the mesial origin of the mesentery, all apparently direct the tip of the ballooning loop towards the left hypochondrium, under the omentum, although pain localization, if any, is to the right lower quadrant The axis of the roentgenographic shadow may be the chief help in the prediagnosis of the loop as cecum As in volvulus of large bowel elsewhere, the roentgenographic appearance is usually characteristic

The term "clockwise" in this study refers to the frontal aspect of the patient, viewed by the examiner.

Derotation and cecopexy, before severe damage occurs, is adequate surgery, the latter necessary because of the liability to recurrence, as suggested in Case 2, and proven in Case 3, of this series. The history of many of these cases indicates that partial torsion with incomplete obstruction is chronic, acute symptoms supervene suddenly. The hypertrophic wall of the ileum proximal to the first twist in Case 2 supports this opinion.

Case 3 is the only volvulus of the cecum we could find in the records of the Cook County Hospital since January, 1936. The patient was not seen by either of the authors, and is discussed at length only because of the excellence of the clinical history and of the proven recurrence.

Midgut volvulus in children occurs in subjects who have a persistent midgut mesentery, with incomplete rotation and lateral fixation of the cecum and ascending colon. Acute intestinal obstruction usually occurs because of volvulus around a band at the hepatic flexure, and, as Ladd³ has so well demonstrated, the cure depends simply on division of this band. In Case 4 prenatal rotation of the colon did not proceed far enough to allow such fixation, hence the preoperative state was similar to the postoperative condition in Ladd's patients operated upon for midgut volvulus. The symptoms were apparently due to mesenteric torsion limited to the ileocecal region—hence, we have included it in this series as a torsion of the cecum, although the anatomic defect might have permitted a twist of the entire midgut.

Case 1—W. V., colored male, age 38, was admitted to Cook County Hospital, at 6 P. M., April 27, 1941, complaining of abdominal pain of 48 hours duration, and repeated emesis for 38 hours. He was intoxicated on admission, and was unable to give a coherent history, or accurately to analyze his present symptoms. He stated that the pain was crampy, diffuse and possibly more intense in the left lower quadrant. He was extremely restless, rolling around in bed. There was slight diffuse rigidity and pronounced tenderness over McBurney's point. The bowel sounds were reduced one half—not obstructive in character. Blood pressure 142/92, pulse 90, temperature 100.4° F, WBC 12,200. *Clinical Diagnosis*: Acute abdominal disease, probably appendicitis. Because of the number of emergency cases scheduled, he was not brought to surgery until six hours after examination in the ward.

Operation—Upon exploration through a right transverse incision (later extended) at the level of the anterior superior spine, cecum and appendix were not found in the right iliac fossa, nor could any ascending colon be identified. There was a small amount of free fluid in the peritoneal cavity and the loops of ileum seen were slightly distended. There was a yielding mass, of about seven inches diameter, in the left upper quadrant. This was cecum, rotated 180° counterclockwise. There was a common ileocolic mesentery, the posterior and lateral attachment of the ascending colon falling in Wolfer's Class V. The attachment of the hepatic flexure was long, it was about this that volvulus occurred. The serosa was glistening, the bowel wall slightly discolored. The loop was untwisted, and a lateral mesentery made by Waugh-type cecopexy. Recovery was uneventful and roentgenologic examination, three weeks postoperative, showed a normally placed, slightly distended colon.

Case 2—L. S., white, female, age 54, moderately obese, was admitted to the

Cook County Hospital, May 15, 1941, with the complaint of abdominal cramps and nausea for 23 hours. She had had repair of an umbilical hernia in 1918, a cholecystectomy in 1929, a ventral hernia repair in 1929, and had used insulin for 10 years. She had a transversely enlarged heart, blood pressure 164/100, vertical right rectus and transverse umbilical scars. Her abdomen was distended, there was no localized tenderness. Bowel sounds were reduced, nonobstructive in character, and she tolerated a two quart enema without increase in pain. Fluoroscopic examination was reported to show distention of entire large bowel, with fluid levels, especially in the cecum. The pain subsided, and she was discharged May 20, 1941.

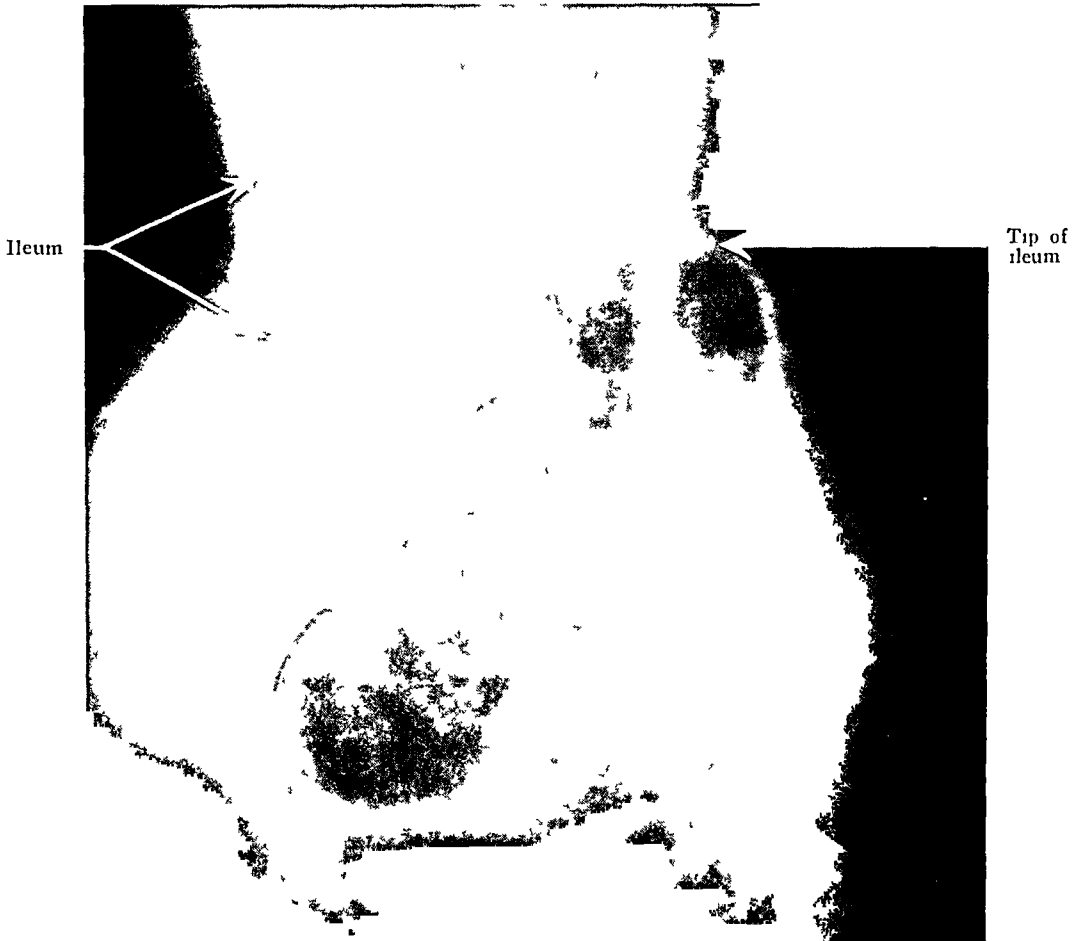


FIG 1—Case 2. Roentgenogram of abdomen showing distended cecum, and double loop of obstructed ileum.

She returned, May 23, 1941, because of a spreading infection of the left foot, and complained that she had no appetite, and had almost constant mild abdominal distress. Her foot was improving and her diabetes was well controlled, when, on June 4, 1941, for "the first time in years," she had two watery bowel movements. Discomfort persisted, and on June 6, 1941, she noted that her abdomen was distended. There was no further stool in spite of repeated enemata. In bed, at 8 A. M., June 8, 1941, she suddenly began to have severe, diffuse, crampy abdominal pain associated with nausea. She vomited once, and felt an urgent desire to go to stool, there was a small formed bowel movement. The pain remained of about the same severity all day, the nausea persisted, and she ate nothing. When examined 12 hours after onset, she was

restless, and complained of cramps and chilliness. She did not appear acutely ill and was afebrile. Her abdomen was markedly and symmetrically distended, there was no rigidity and only slight generalized tenderness. Bowel sounds were absent. No masses or herniae were found. Twelve hundred cc of the two quart enema was retained, with no increase in pain, and returned with no fecal material or gas. The roentgenogram of the abdomen is shown in Figure 1. Upon the history, and this finding, the diagnosis of volvulus of the cecum was made. The WBC was 14,000, Hb 80%. The urine contained a heavy trace of albumin.

Operation—Under spinal analgesia, 15 hours after onset, about 500 cc of blood-tinged fluid escaped through a right rectus incision. The distended cecum and ascending colon was 15 cm in diameter, 25 cm in its long axis. The wall was uniformly red-black in color, the serosa still glistening. It was rotated clockwise 540° on its longitudinal axis (with ileum looped twice about it), 180° in the sagittal and about 60° in the frontal plane. There was a common ileocolic mesentery, a firm adhesive band from the right bium of the pelvis to the mesentery of the ileum, eight centimeters from the ileocecal valve, about which rotation occurred. There was marked hypertrophy of the wall of the terminal 10–12 cm of ileum. The lateral mesenteric attachment of the ascending colon extended only four centimeters down from the hepatic flexure. Twenty minutes after detorsion, during which oxygen was administered, and warm towels applied to the bowel, the color of the segment was unchanged. Proximal ileum and distal ascending colon were gun-barreled, the mass exteriorized, and the wound closed around it.

There was slight abdominal distention 24 hours later; this had disappeared at 48 hours, and her abdomen was scaphoid, bowel sounds were heard 8–10 per minute. The cecum was opened by cautery on June 10, 1941. Her heart remained rapid, there was severe cough, she developed many pulmonary râles, and died June 12, 1941, four days postoperative, of cardiovascular failure and pulmonary edema. The wall of the exteriorized bowel remained red-black but not necrotic.

Case 3—M. C. white, female, age 38, married, was admitted to the Cook County Hospital at 8 P. M. October 24, 1938, complaining of crampy pain in the lower abdomen and sacral region for three and one-half days, obstipation for six days, and vomiting one day. She stated she had been perfectly well until two years previously, when she had been in the hospital for similar symptoms, which lasted three days. At that time she had had an operation for "twisted bowels." There had been no illness in the interim. At 2 P. M. October 21, 1938, two hours after a light lunch, she had a sudden, sharp epigastric cramp. She remained at her work until 8 P. M., and noted recurrence of the cramps about every two hours. She had had two stools with difficulty during the previous three days, and tried to move her bowels—thinking her trouble was constipation. She slept fairly well, and worked all the next day. The pains became more severe, longer and more frequent. She ate nothing until 7 P. M. There was no increase in the distress on eating a light supper. No vomiting or bowel movement all day. She did not sleep that night because of the pain. By 9:30 A. M., October 23, 1938, the pain was diffuse, continuous and severe, and she noted severe, continuous sacral backache. Both pains had exacerbations every 15–20 minutes. She remained in bed all day, took no food, had no vomiting or bowel movement. She did not sleep. At 10:00 A. M. October 24, 1938, she became nauseated, vomited a little clear fluid and remained nauseated all day, until admission to the hospital. The past history was otherwise irrelevant.

The patient was a well-developed, well-nourished white female, moving restlessly about the bed. Temperature 100° F, respirations 22, blood pressure 150/100. WBC 10,200. Urine normal. The abdomen was extremely distended. There was a lower right rectus scar. The liver, kidneys and spleen were not felt, nor were any masses or herniae found. There was slight tenderness on deep pressure, and slight voluntary

rigidity in the right lower quadrant. There was no rebound tenderness, 4-6 low-pitched bowel sounds were heard each minute. Fluoroscopy, at 11 45 P M, was reported as follows: "Chest negative, right diaphragm high. Liver shadow partly obscured by marked gaseous distention of a loop of large bowel, with considerable fluid apparently sigmoid volvulus" (Fig 2)

Operation—It was impossible to get the old chart. A diagnosis of volvulus of the sigmoid was made, and at 3 25 A M the abdomen was opened through a lower left rectus incision, under spinal analgesia. The cecum was enormously dilated, filling the abdomen from pelvis to diaphragm, the torsion was 360°, clockwise, the appendix wound around the twist. The wall of the cecum was viable. Detorsion and deflation by pressure, and a long rectal tube, were followed by fixation of the cecum to the lateral peritoneum and to that in the wound, and by tube cecostomy.

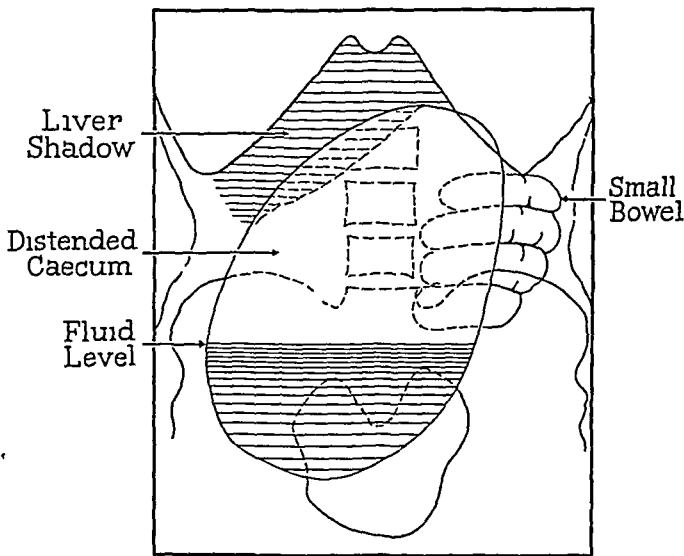


FIG 2—Case 3 Intern's drawing of appearance of abdomen at fluoroscopy

The postoperative course was uneventful, she was discharged 18 days postoperative, with only slight and occasional drainage from the cecostomy.

The chart from the previous admission disclosed that, on September 5, 1936, she had been found to have a 180° volvulus of the cecum, simple detorsion had been effected, and she left the hospital September 17, 1936.

Case 4—L B, white, male, age 34, was admitted to the Oak Park Hospital at 4 30 P M, June 18, 1941, complaining of colicky, right lower quadrant pain of four hours duration. The onset was sudden, with sharp, crampy pain in the right loin extending over the iliac crest to the right lower quadrant but not to the scrotum. Weakness, sweating, nausea and vomiting accompanied the paroxysms of pain during which he threw himself around the bed. There had been no urinary symptoms. He stated that he had had numerous similar attacks (during one of which, in 1937, his appendix had been removed), but none so severe as the present one. *Physical Examination*—Blood count and intravenous pyelogram were all negative. The retrograde pyelogram was negative. There was slight tenderness on deep pressure in the right lower quadrant. Bowel sounds were normal, except that twice during paroxysms, a few obstructive borborygmi were heard. Gastro-intestinal roentgenograms, five days later, revealed elongation and angulation of the second and third portions of the duodenum, a left-sided right colon with small bowel to the right of it, and obstruction in the terminal ileum (Figs 3 and 4).

VOLVULUS OF CECUM

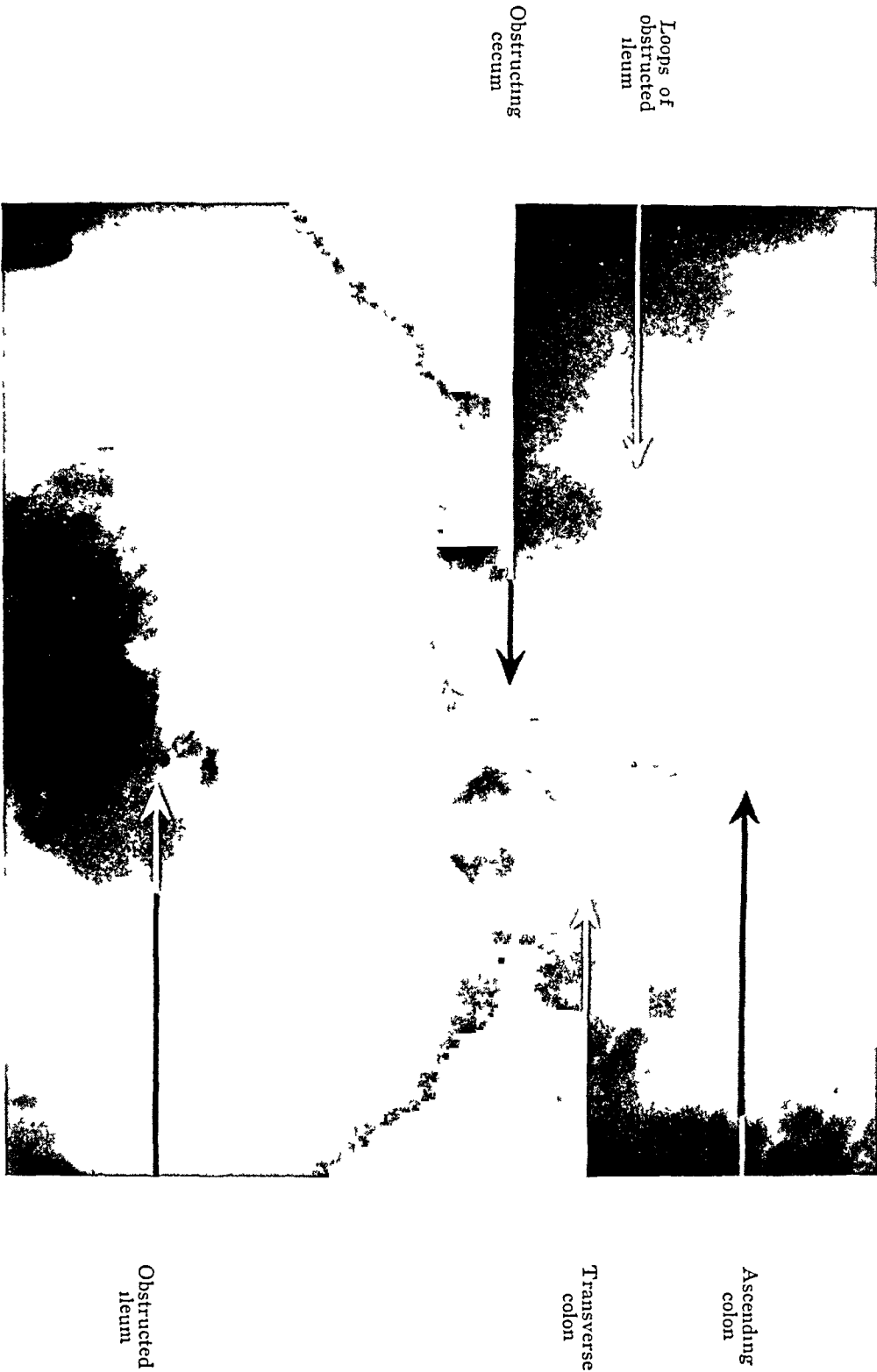


Fig. 3—Case 4 Roentgenogram of abdomen showing left sided colon Central gas filled cecum and obstructed ileum at A

Operation—June 24, 1941 Through a right rectus incision, the cecum was found lying free in the lower abdomen. It was edematous and thickened. The transverse mesocolon and omentum ended at the midcolic artery. The right colon and small bowel were on a common mesentery which was not fixed except at its root. Most of the small bowel was in the right abdomen. The terminal ileum was hypertrophic, coming in from the right, it was kinked by adhesions to the anterior tenna of the cecum.



FIG. 4.—Case 4. Six hours after barium by mouth. A Left sided colon
B Right sided small bowel C Gas bubble in terminal ileum encircling cecum

The redundant cecum and ileum were gun-barreled and exteriorized, after suturing the ascending colon to the anterior peritoneum for a distance of 10 cm, the wound closed with interrupted sutures. A 15 cm-long segment was removed by cautery July 2, 1941, and a Devine spur-crushing clamp applied. This came off July 6, and he was discharged July 14, 1941. On July 24, 1941, the bowel ends and skin were closed, he was discharged July 31, 1941. On January 30, 1942, the large ventral hernia remaining, was repaired with a free fascial graft, there was primary wound healing on discharge, February 10, 1942. He returned to full work as a fireman, April 1, 1942, and he has remained well. No colic has occurred since the first operation.

This rather cumbersome staged-procedure was adopted as the most logical method of dealing with a free redundant midgut, which could not be fixed in anything approaching normal position, yet which required fixation that would not allow herniation through apertures or over bands. Hence an attempt to fix it at the hepatic flexure or along the right lateral gutter was judged impossible because of the absence of the right half of the transverse mesocolon and the deformity at the duodenojejunal juncture.

SUMMARY Four cases of torsion of the cecum are reported. All but the first had more than one attack, one had been operated upon previously for the same condition. The rather leisurely, colicky course after the onset of acute pain, and the operative findings suggest that vascular damage is late, and occurs mainly from distention of the loop. The distended loop of colon seen in the plain films can be recognized as cecum.

CONCLUSION

1. Volvulus of the cecum occurs only in the presence of malfixation of the cecum. It is probably chronic or recurrent, and obstructive episodes are due to physiologic aberrations, primarily intestinal.

2. The early symptoms are mild, progress is slow, characterized by increasingly severe colic, and signs of intra-abdominal inflammation are late.

3. Diagnosis depends upon the symptoms of bowel obstruction and characteristic roentgenologic findings.

4. Fixation of the abnormally mobile segment is necessary to prevent recurrence. The present treatment of midgut volvulus in children may not prevent a later twisting on a different axis.

REFERENCES

- ¹ Bundschuh, E. Volvulus of the Cecum. *Beit z klin Chir*, **85**, 58, 1913.
- ² Wolfer, John A., Beaton, Lindsay E., and Anson, Barry J. Volvulus of the Cecum. Anatomic Factors in its Etiology. *Surg Gynec and Obst*, **74**, 882, April, 1942.
- ³ Ladd and Gross. *Abdominal Surgery of Infancy and Childhood*. W. B. Saunders Co., Philadelphia, 1941. Pp. 62-69.

LEIOMYOSARCOMA OF THE UTERUS

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AMONG THE RARE SARCOMAS OF THE UTERUS, those of myomatous structure predominate. There have been rather extensive reviews in the past associated with the publication of one or more case reports. Knott,¹ in 1901, collected 118 cases, and quotes Williams as having found 144 sarcomas of all varieties. In 1905, Pequand² wrote a comprehensive treatise on all forms of uterine sarcoma. He described 41 which arose from the mucosa or the parenchyma. Many articles have accentuated the discrepancy between the histologic changes and the clinical course. Certain authors have pointed out the lack of accuracy of morphologic diagnosis. Others have emphasized the use of special histologic criteria alone. There has been some controversy over their origin, whether primary or a secondary sarcomatous change in a preexisting leiomyoma.

With these ideas in mind, it is the object of this paper to outline the alterations indicative of cancer. There will be included a discussion of the incidence, the ratio to uterine carcinoma, the location in the uterus, and the gross and microscopic findings. The cytologic structure will be emphasized. The material used as the basis for the investigation consists of surgical and autopsy specimens. No clinical correlation or follow-up study has been attempted.

In the pathologic files of the New England Deaconess Hospital there are 35 leiomyosarcomas of the uterus, 33 from surgical specimens and two from necropsies. In addition, there are sections from two postmortem examinations, in which death was the result of metastatic leiomyosarcoma, with probable origin in the uterus. The uteri in these two cases had been removed in other hospitals, presumably for tumor. These cases are included because they will raise the incidence of leiomyosarcoma of the uterus discovered at necropsy in this hospital to the usually accepted figure determined by analysis of surgically excised specimens.

Excluded from the above group are 113 tumors (111 operative specimens and two from autopsies) which have been diagnosed as leiomyosarcoma of the uterus, clinically benign. These will be discussed later.

The routine stains used were hematoxylin and eosin on alcohol-formalin-fixed and celloidin-embedded material or eosin-methylene blue and Mallory's phosphotungstic acid-hematoxylin on Zenker's fixed blocks. Many specimens were stained by all methods, while some were treated with hematoxylin and eosin only. Since the celloidin-embedded sections were thicker than the others, hence more suggestively cellular, it was necessary to evaluate them with greater care. Use of one of the routine connective tissue stains will facilitate diagnosis.

Because of the personal factor, attempts to grade tumors are often unsuccessful. Nevertheless, with reasonably impartial study, it was possible to divide the material into three specific groups. By histologic data alone the 35 leiomyosarcomas already mentioned were classified as follows: 20 were Grade III (all surgical) and 15 were Grade II (13 surgical, and two autopsy). The 113 cases mentioned above as clinically benign were listed as Grade I.

The criteria by which leiomyosarcomas are placed in Grade III are

- 1 Cellularity Marked in 11, moderate in 8, and slight in 1
- 2 Mitoses Marked in 16, moderate in 4
- 3 Pleomorphism Marked in 6, moderate in 5, and slight in 9
- 4 Bizarre nuclei Marked in 7, moderate in 6, and slight in 7
- 5 Hyperchromatism Marked in 7, moderate in 7, and slight in 6
- 6 Increased nuclear-cytoplasmic ratio Marked in 11, moderate in 5, and slight in 4
- 7 Loss of pattern or architecture Marked in 10, moderate in 6, and slight in 4
- 8 Anaplasia Marked in 7, moderate in 4, and slight in 9
- 9 Multinucleation Marked in 4, moderate in 6, and slight in 10
- 10 Tumor giant cells Marked in 4, moderate in 5, and slight in 11
- 11 Invasion Marked in 7, moderate in 4, and slight in 9
- 12 Preservation of capsule Marked in 3, moderate in 10, and slight in 7
- 13 Gradation between tumor and uninvolved tissue Marked in 5, moderate in 4, and slight in 11
- 14 Retention of fibrous elements Marked in 2, moderate in 5, and slight in 13
- 15 Vascular splits Marked in 5, moderate in 5, and slight in 10
- 16 Blood vessel invasion Contrary to the usual teaching none was found. However, routine Weigert stains were not made.
- 17 Degeneration Marked in 4, moderate in 11, slight in 5
- 18 Necrosis Marked in 4, moderate in 9, slight in 7
- 19 Cystic change Marked in 1, moderate in 3, slight to none in 16
- 20 Metastases In one only, to an ovary. It may be possible to say that an additional one showed metastases to the lungs and pleura, as she was autopsied somewhat over seven years later and presented disease in these viscera.

Obviously, these changes were not present in all tumors to the same degree, but a sufficient number, characteristic of rapid growth and invasiveness, were found to indicate their being placed in Grade III. Macroscopically, 10 of the 20 Grade III neoplasms were the only uterine tumors, and 10 were associated with multiple leiomyomas. Except for the three considered by us to be primary in origin, there was no tendency to occupy any specific muscle coat. These three primary tumors were single, small, soft, submucosal, and occupied the fundus. On microscopic section, they contained immature muscle cells with little stroma. The other 17 Grade III sarcomas were thought to have originated in leiomyomas already present. The sarcomatous transformation occurred in intramural tumors without regard to their orientation in the uterus. They were soft to moderately firm, often poorly encapsulated, necrotic or cystic, bulky, reddish-brown, yellowish-brown, gray or white, sometimes hemorrhagic, smooth and homogeneous, and bulged above the cut surface.

Fifteen cases were placed in Grade II. Thirteen were obtained from operative specimens and two from necropsies. All were thought to be derived

from preexisting leiomyomas. As in Grade III, no predilection of site was apparent. In four of the cases the leiomyoma which underwent sarcomatous change was single. In the remaining 11 there were many leiomyomas besides the one which became malignant.

Grossly, these showed little evidence of malignancy. There was some minimal cystic change, the capsule was thin, and the center was soft.

The data used for placing these cases in Grade II are

- 1 Cellularity. Moderate in 5, slight in 8, minimal in 2
- 2 Mitoses. Marked in 2, moderate in 12, slight in 1
- 3 Pleomorphism. Marked in 3, moderate in 10, slight in 2
- 4 Bizarre nuclei. Marked in 2, moderate in 12, slight in 1
- 5 Hyperchromatism. Marked in 5, moderate in 10
- 6 Increased nuclear-cytoplasmic ratio. Moderate in 3, slight in 8, absent in 4
- 7 Loss of pattern or architecture. Moderate in 10, slight in 5
- 8 Anaplasia. Moderate in 1, slight in 4, minimal in 5, absent in 5
- 9 Multinucleation. Marked in 3, moderate in 3, slight in 9
- 10 Tumor giant cells. Marked in 3, slight in 7, absent in 5
- 11 Invasion. Moderate in 3, slight in 2, absent in 10
- 12 Preservation of capsule. Marked in 10, moderate in 3, slight in 2
- 13 Gradation between tumor and uninvolved tissue. Moderate in 8, slight in 5, absent in 2
- 14 Retention of fibrous elements. Marked in 6, moderate in 8, slight in 1
- 15 Vascular slits. Moderate in 3, slight in 7, absent in 5
- 16 Blood vessel invasion. None
- 17 Degeneration. Marked in 1, moderate in 2, slight in 9, absent in 3
- 18 Necrosis. Moderate in 3, slight in 1, minimal in 4, absent in 7
- 19 Cyst formation. Four only showed this change, usually of minimal degree
- 20 Metastasis. None

By a survey of the above, the better differentiated leiomyosarcomas are less cellular, have a lower nuclear-cytoplasmic ratio, fewer mitoses and tumor giant cells, and, in general, show closer resemblance to a leiomyoma. They are what some authors describe as "spindle-form" sarcomas. In our opinion, however, the use of the descriptive terms, "spindle and round cell," is valueless because of their generality.

The remaining 113 cases listed as Grade I, and diagnosed as leiomyosarcoma, clinically benign, require clarification. Grossly, these are leiomyomas. On routine microscopic study, none the less, they show an increased number of normal and abnormal mitoses, increased cellularity, foci of pleomorphism, hyperchromatism, and tumor giant cells, and minimal loss of the normal parallelism of fibers. With such alteration from the usual character of leiomyoma, it is not possible to include them as benign tumors. Since it is necessary to diagnose them pathologically as either benign or malignant, the term has been selected to indicate both histologic picture and clinical course. It is possible that by routine section a less malignant portion of the tumor may have been studied, while other regions may have been more anaplastic.

DISCUSSION.—The diagnosis of leiomyosarcoma is histologic, and depends upon the correct interpretation of morphologic evidence. Leiomyomas

of the uterus are so common that familiarity with them tends to foster carelessness. Accurate study presupposes that each one is at least exposed to view by cutting into it. If not too numerous, a section of each one should be studied microscopically. When such a procedure is not feasible because of the multiplicity, any which grossly present some deviation from the usual pattern ought to be investigated histologically. Special care must be given the solitary, small, submucosal variety.

Any leiomyoma found at postmortem examination, and in which there is macroscopic change indicative of sarcoma, should be studied histologically. In occasional autopsies there are sarcomatous masses of smooth muscle formation in organs such as the lungs, brain, intestine, and pleura. Often there has been a former subtotal or total hysterectomy. In these cases it may be assumed that the primary source of the new growth was in this excised tissue.

Regarding the incidence, both Vogt³ and Buntent⁴ have charted the results of various reports. Nearly all who have published series of any size have made a point of emphasizing the infrequency of this neoplasm. We have used only the 35 leiomyosarcomas of Grades II and III in the determination of incidence. During the period studied, there were 2,600 leiomyomatous uteri—2,321 from surgical specimens, and 279 occurring in 2,830 necropsies. This gives an incidence of 1.35% which is comparable to that obtained by most of the other writers. But if we include the 113 which are clinically benign, the figure rises to 5.6%. This is in agreement with Unbehau,⁵ who quotes Imhauser as having a frequency of 5.3% sarcomatous change in all myomas operated upon between 1918 and 1923. When he adds questionable sarcomas, it is 7.7%. For his statistics Imhauser adds the two series above and obtains an average of 6%. Unbehau also reviewed the sarcomas seen between 1923 and 1932 at the same clinic. There were 11 out of 208 operable myomas with a resultant incidence of 5.3%. Miller and Rogers⁶ reviewed the uterine sarcomas at the Massachusetts General Hospital between 1876 and 1926, and found 25 in 2,043 leiomyomatous uteri, or an incidence of 1.2%. Proper and Simpson⁷ describe 22 malignant leiomyomas out of 357 leiomyomas, an incidence of 6%. Novak and Anderson⁸ have analyzed 26,973 uterine specimens. Their incidence, using 59 cases, was 0.22%. Hanley and Howkins⁹ estimate that sarcoma represents 1% of the mesodermal tumors of the uterus and 2% of uterine malignant tumors.

Klaften and Naviatil¹¹ report 44 cases of sarcoma of the uterus observed between 1921 and 1934. Thirty-six arose in the body of the uterus, 25 in fibromyomas. During the same period there were 1,755 carcinomas.

Despite the high figures of Unbehau⁵ and Proper and Simpson,⁷ most writers accept an incidence of 1 to 2%. The difference may lie in the inclusion of those cases placed in our Grade I group.

Haase¹⁰ concludes that 15 of every 100 gynecologic patients have malignant tumors. He describes 53 sarcomas, of all sites, in the female generative tract. There were 38 in the uterus, 32 in the body, and six in the cervix, 35 were of the wall and three of the mucosa.

The ratio of sarcoma to carcinoma is quoted as 1 40 or 50. During the period of time when the sarcomas were seen here, there were 1,520 carcinomas of the uterus, hence, our ratio is 1 43. This was computed by using the sarcomas of Grades II and III alone.

These observations scarcely justify Coiscaden's¹² statement that "the development of sarcoma in a myoma is to me an academic and not a clinical problem. Despite the report of bizarre microscopic pictures, called sarcoma by many investigators of myomatous tissue, the autopsy rooms still remain as empty of women dead of sarcoma of the uterus as they did in the days before hysterectomy was so universally performed."

Further evidence against the accuracy of the above remark is added by the following. Five of Miller and Rogers'⁶ 25 cases were known to have died of the disease, with half of them untraced, 10 of Searight's¹⁶ 12 cases died of sarcoma either local or metastatic, and 16 of Kimbrough's 35 cases were proved to be dead of the lesion.

In contrast to Coiscaden,¹² Masson¹⁴ offers what is a more correct impression, *ie* "With complete records it would be possible to show that many women have died as the result of recurrent pelvic tumors following myomectomies and semiradical operations for tumors which were diagnosed benign."

Most writers, who have acknowledged the origin of leiomyosarcoma in a nonmyomatous uterus, agree that such sarcomas are small, soft, submucosal, superficially eroded, and fundal in location. Histologically, the cells are more numerous, lie in less abundant stroma, show more marked anaplasia, and greater nuclear-cytoplasmic ratio, and, in general, are more immature. Wolfe¹⁵ says if they are submucosal, they are primary, if interstitial, they are secondary to leiomyomas. Kimbrough¹³ concludes, on rather inadequate data, that primary sarcoma is three times more malignant than those which arise in leiomyomas.

There is no more known concerning the origin of leiomyosarcomas than there is regarding the development of neoplasms elsewhere in the body. Cohnheim's test-theory is suggested by some. Searight¹⁶ thinks that they may arise from any of the mesodermal elements making up the uterus, and includes those from the muscle or connective tissue of the uterine wall, those originating in myomas of either the corpus or the cervix, and those starting in the blood vessel wall. Reel and Chailton¹⁷ believe, contrary to most pathologists, that the sarcoma cells arise from a metaplasia of the connective tissue cells of a fibromyoma.

Regarding their development, Neely¹⁸ states that "in the pregnant uterus new muscle cells are formed by differentiation of the small, round, undifferentiated mesenchymal cells found normally between the muscle bundles"

"this undifferentiated muscle cell is multipotential"

Pequand,² who studied the subject as a whole quite thoroughly, considered that nearly always the leiomyosarcoma resulted from the malignant transformation of a fibroleiomyoma. He recognized, however, that the sar-

comas could arise in the parenchymal smooth muscle without any known preexisting tumor. He listed the following theories of origin:

- 1 Proliferation of intramuscular connective tissue (neoplasms were actually fibrosarcomas)
- 2 Proliferation from blood vessel or lymphatic walls
- 3 Development of sarcoma cells from transformation of muscle fibers

Regarding the gross characteristics, we have already recorded the criteria which we believe to be indicative of leiomyosarcoma either primary or arising in a leiomyoma:

The following peculiarities may indicate malignancy in a leiomyoma:¹⁹

- 1 Unusual friability of the broad ligaments
- 2 Remarkable vascularity of the tumor
- 3 Absence of a sharp line of demarcation between the tumor and the myometrium
- 4 Difficulty in shelling out the tumor from its apparent circumscribed limits
- 5 An opaque appearance on section
- 6 An edematous and sparsely fasciculated appearance of the cut surface which is softer than that of a fibromyoma

Many of the above characteristics are applicable to pathologic study. Nearly all writers include softening of a leiomyoma, change or lack of color, fusion with parametrium, extension into adjoining uterus, homogeneity of cut surface, necrotic or cystic foci, loss of characteristic silky hue of the leiomyoma, preponderance of involvement of body, and association with multiple leiomyomas.

Evans²⁰ has emphasized the histologic changes more than any other writer. He gives the composite picture of microscopic malignancy in the following outline:

- 1 Increase in size of tumor cells as compared with normal muscle or benign muscle tumor cells
- 2 Shorter and plumper cells with nuclei more nearly oval than normal muscle or benign muscle tumor cells, round and "vesicular nuclei"
- 3 Inequality in size and irregularity in shape and arrangement of the cells
- 4 Lack of "differentiation" of cells
- 5 Unequal staining of nuclei and deeply-staining nuclei
- 6 Presence of immense cells (protoplasmic plaques) with hyperchromatic, single or multiple nuclei (giant cells)
- 7 Presence of mitotic figures, typical and atypical
- 8 Decrease or absence of stromal fibers between the cells
- 9 Thinness or absence of vessel walls

His study is based upon analysis of 72 cases diagnosed as "sarcomatous," "cellular" or "very cellular fibromyomatous tumors—in about 4,000 operations for the cure of uterine fibromyomata." By use of the above material he made a chart of the number of mitotic figures seen in 100 microscopic fields of a 1/12th immersion lens and graded the tumors accordingly. He tabulated his findings as:

13 cases	2,200–12,000	mitotic figures for each cubic millimeter
12 cases	200–800	mitotic figures for each cubic millimeter
47 cases	0–few	mitotic figures for each cubic millimeter

Many writers have had recourse to this method, and have substantiated his work. His less malignant grade may well correspond to our group

which is called clinically benign

Novak and Anderson,⁶ also, used the number of mitoses in order to group their cases, although they used five divisions 0-5 mitoses, 6-10 mitoses, 11-20 mitoses, 21-30 mitoses, and 30-88 mitoses. They utilized the chart as a prognostic as well as a diagnostic procedure. Death occurred more frequently, and earlier, in the cases where the tumor showed the highest number of mitoses.

Despite the implied accuracy of the above analyses, it is not conducive to place too much reliance upon one histologic feature alone. We believe that many of the morphologic alterations mentioned by us are just as reliable. Certainly, cellularity, increased nuclear-cytoplasmic ratio, loss of pattern, and/or invasion, if utilized in a similar fashion, would be of equal value in the microscopic diagnosis.

We disagree definitely with Corscaden and Stout²¹ who "discount the ability to recognize malignancy in this type of new growth (sarcoma of the uterus) by means of the microscope alone." They insist upon the finding of infiltration, metastases or recurrence after removal. Actually, such changes are manifestations of advanced malignancy and have no place in the present-day ideas of neoplastic disease.

In most instances the diagnosis of leiomyosarcoma is usually made upon tissue which has already been excised. Thus, there is no indication for alteration in the surgical procedure. To know of the existence of a leiomyosarcoma is of definite prognostic value, however. Since leiomyosarcomas are somewhat radioresponsive, radiation therapy may be indicated. If the surgeon has performed a subtotal hysterectomy, he may wish to resect the residual cervix.

There is little to be said concerning the preoperative diagnosis of these tumors. Tietze and Meiser²² have given special attention to the diagnosis of uterine sarcoma by biopsy. They stress the marked irregularity of cell size, giant cells, inequality of nuclei, variability of nuclear shape and chromatin content, increase in mitoses and poorly developed stroma. Actually, only a small number of submucosal leiomyosarcomas presenting through the endometrium are accessible to study by curettage. Thus, too much reliance should not be placed on this method.

Because Vogt's³ series showed associated inflammatory lesions in one or both adnexa in 50% of the cases, we reviewed our series to see if we could find similar changes. We could not substantiate this impression. No other writer makes any comment either one way or the other.

Only one of our cases came to autopsy. It presented metastases to the lungs, pleuras, ribs, and pelvic tissue. Both blood vessel and lymphatic invasion were seen. According to the authors who have studied postmortem material the lungs, pleura and brain are most commonly the seat of secondary spread. There is usually fairly widespread local invasion into the adnexa, urinary bladder, small intestine, and rectum. In one of our surgical specimens a metastasis was found in one ovary.

As the intention of this paper has been to stress the pathologic phase, no attempt is made to include clinical data. Those who are interested may review any of a number of articles on the subject, some of which are included in our bibliography.

SUMMARY—All leiomyosarcomas of the uterus secured from surgical material and autopsies in the Laboratory of Pathology of the New England Deaconess Hospital have been reviewed.

By a chart giving the necessary microscopic data for the pathologic diagnosis, these leiomyosarcomas were divided into three groups on the basis of relative malignancy—20 were Grade III, 15 were Grade II, and the remaining 113, called “clinically benign,” were placed in Grade I.

The gross changes indicative of leiomyosarcoma are listed.

The incidence of leiomyosarcoma and its ratio to carcinoma is determined, and coincides with that reported by most writers.

Although leiomyosarcomas of the uterus may be primary, they most commonly arise secondarily in preexisting leiomyomas.

Theories concerning the methods of histogenesis are given.

The presence of leiomyosarcomatous nodules in various organs of obscure necropsies, in which no primary source is determined and in which the uterus is surgically absent, suggests the spread from what was a sarcoma of myomatous origin in the uterus.

A correct diagnosis of leiomyosarcoma of the uterus can be made morphologically, and it does not require the additional confirmation of invasion, metastasis and/or recurrence.

A general discussion of the lesion is included, with especial reference to the pathologic data.

CONCLUSIONS

1 The diagnosis of leiomyosarcoma of the uterus is made by histologic study only, and three grades of malignancy can be recognized.

2 Leiomyosarcoma of the uterus may result in death despite treatment.

3 The incidence of leiomyosarcoma of the uterus is 1 to 2%—1.35% in the present series of uteri with leiomyomas.

4 The ratio of leiomyosarcoma to carcinoma of the uterus is 1:40 or 1:50, 1:43 in this series.

5 We interpret three of our cases as being of primary origin and the rest as being secondary in preexisting leiomyomas.

6 Finally, we believe that in any necropsy showing metastases of leiomyomatous structure in the lungs, pleura, brain or pelvic tissues, and in which the uterus is absent (having been removed surgically), the primary source is probably a leiomyosarcoma of the uterus.

BIBLIOGRAPHY

- ¹ Knott, van Buren. Sarcoma of the Uterus. *ANNALS OF SURGERY* 33, 137, 1901.
- ² Pequand, G. Le Sarcome de l'Uterus, Anatomie Pathologique des Sarcomes du Col. *Histogenese. Rev. de gynec. et de chir. abd.*, 9, 579, 1905.

- ³ Vogt, Marietta E Sarcoma of the Uterus Report of 30 Cases Am J Obst & Gynec, 5, 523, 1923
- ⁴ Bunten, J C Sarcoma of the Uterus Surg, Gynec & Obst, 41, 470, 1925
- ⁵ Unbehaun, Gerd Über die Häufigkeit des Sarcoma Uteri Klin Wchnschr, 11, 1152, 1932
- ⁶ Miller, R H, and Rogers, Horatio Sarcoma of the Uterus New England J Med, 198, 927, 1925
- ⁷ Proper, Mina S, and Simpson, Burton T Malignant Leiomyomata Surg, Gynec & Obst, 29, 39, 1919
- ⁸ Novak, Emil, and Anderson, David Fyfe Sarcoma of the Uterus Am J Obst & Gynec, 34, 740, 1937
- ⁹ Handley, R S, and Howkins, John Sarcoma of the Uterus Lancet, 2, 1246, 1937
- ¹⁰ Haase, W Zur Pathologie der Sarkome weiblicher Geschlechtsorgane besonders der Gebärmutter Ztschr f Geburtsh u Gynak, 102, 344, 1932
- ¹¹ Klaften, E, and Navratil, E Über Sarkome des Uterus und der Vagina Zentralbl f Gynak, 58, 2170-2188, September, 1934
- ¹² Corscaden, James A The Selective Treatment of Fibromyoma of the Uterus New York State J Med, 27, 1129, 1927
- ¹³ Kimbrough, Robert A Sarcoma of the Uterus Am J Obst & Gynec, 28, 723, 1934
- ¹⁴ Masson, James C Sarcoma of the Uterus Am J Obst & Gynec, 5, 345, 1923
- ¹⁵ Wolfe, Samuel A Mural Sarcoma of the Uterus Am J Obst & Gynec, 23, 232, 1932
- ¹⁶ Searight, William Sarcoma of the Uterus South M J, 34, 326, 1941
- ¹⁷ Reel, Philip J, and Charlton, Paul H Sarcoma of the Uterus ANNALS OF SURGERY, 77, 476, 1923
- ¹⁸ Neely, J Marshall Sarcoma of the Uterus Arch Path, 23, 525, 1937
- ¹⁹ Dannreuther, Walter T Leiomyosarcoma of the Uterus J A M A, 91, 1532, 1928
- ²⁰ Evans, Newton Malignant Myomata and Related Tumors of the Uterus Surg, Gynec & Obst, 30, 225, 1920
- ²¹ Corscaden, J A, and Stout, A P Sarcoma of the Uterus Am J Roentgenol, 21, 155, 1929
- ²² Treite, P, and Meiser, A Ein Beitrage zur Pathologie des Uterussarkomes unter besonderer Berücksichtigung seiner mikroskopischen Diagnostik aus Probeteilschen Zentralbl f Gynak, 64, 593, 1940

LESS COMMON LESIONS OF THE ASTRAGALUS

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CASUAL REFLECTION on pathology occurring in the astragalus might well lead one to the erroneous conclusion that it is practically limited to the direct results of trauma, and to infection secondary to involvement of the ankle joint. That the variety of lesions to which the bone is subject is actually rather wide is shown by the following eight cases, which seem interesting in themselves, besides being of value in establishing this point.

CASE REPORTS

Case 1—J McK, C-110-892, male, age two, was brought to the clinic, November 7, 1935 with the left ankle and foot in a plaster encasement, and a history of having been treated at St Agnes Hospital for tuberculosis of the ankle.

Examination showed a healed sinus tract on the inner aspect of the ankle. There was no swelling or tenderness, and there was free motion. Roentgenologic examination showed an irregular area of bone destruction in the neck of the astragalus, with no surrounding bone reaction, and with some thickening of the soft tissues of the ankle joint (Fig 1). *Provisional Diagnosis* Tuberculosis.

Course The plaster encasement was left off, and the patient was followed in the clinic until September, 1936, without any return of symptoms. Supplementary information (through the courtesy of Vanderbilt Clinic). The patient was followed at Vanderbilt Clinic from June, 1938, to the present. In 1940, he developed an ulcer over the site of an old scar. This healed in a few weeks. Culture at that time did not reveal tubercle bacilli. The Mantoux test was positive on two occasions. The boy is well and has no complaints at the present time.

Past History (from the Vanderbilt Clinic records). In 1934, the patient was taken to Morrisania Hospital. Aspiration done at that hospital demonstrated tubercle bacilli. From Morrisania Hospital the boy was sent to St Agnes Hospital for convalescence, whence he came to the Hospital for Ruptured and Crippled in 1935.

Established Diagnosis Tuberculosis.

Case 2—R C, C-149-816, male, age seven, was brought to the clinic with the history that four months previously he had hurt his ankle. A few days later there was pain and swelling, with temperature rise. The family physician made an incision over the lateral malleolus—pus was found. The symptoms subsided and he went about with a limp until two days ago, when the swelling and pain recurred.

Examination at this clinic showed much swelling about the ankle. A roentgenogram showed tremendous soft tissue swelling, with extensive destructive changes in the posterior portion of the astragalus (Fig 2). The condition was thought to be tuberculosis. Ten cubic centimeters of yellow fluid was aspirated, a plaster encasement applied, and the patient was instructed to return in six weeks. Smears of the aspirated fluid showed pus cells but no organisms, culture showed *Staphylococcus aureus*, guinea-pig injection was negative for tuberculosis.

Established Diagnosis Staphylococcus osteomyelitis of the astragalus, with involvement of the adjacent joints.



FIG 1—Case 1 Tuberculosis of the astragalus



FIG 2—Case 2 *Staphylococcus aureus* infection of the astragalus and adjacent joints

Course Surprisingly enough, the patient made a rapid and uneventful recovery, with no treatment other than the diagnostic aspiration and plaster immobilization. At the end of a year the condition seemed healed or entirely quiescent both clinically and roentgenologically.

Case 3—F S, X-ray No 37-5063, male. This was a Workmen's Compensation case, seen only once in the Emergency Room, with a clinical diagnosis of strain of the ankle. The roentgenographic findings were entirely characteristic of osteochondritis dissecans of the astragalus (Fig 3).



FIG 3—Case 3 Osteochondritis dissecans of the astragalus

Case 4—A B, X-ray No 38-0177, female, age six. Patient was struck by a car, injuring ankle, and was treated in a plaster encasement in another hospital for about seven weeks. Roentgenologic examination, about 2½ months after injury, showed aseptic necrosis of the body of the astragalus, with crushing of the body, probably secondary to the circulatory disturbance rather than produced by the original injury (Fig 4). Patient was treated conservatively, and was seen only for a short time.

Case 5—A M, C-130-170, male, age 14, came to the clinic with complaint of weakness of the left foot, and bony enlargement just anterior to the external malleolus. Examination revealed a large rounded bony mass just anterior to the external malleolus, apparently attached to the astragalus. Roentgenologic examination, from a number of different angles, showed a body with structure of cancellous bone lying lateral to the head and neck of the astragalus, above the anterior extremity of the calcaneus and proximal portion of the cuboid bone. This bony body was not attached to the calcaneus or cuboid bone, but seemed definitely attached to the astragalus (Fig 5).

The patient did not return, and no final diagnosis was made. However, there seems little doubt that the condition was an osteochondroma, arising from the astragalus.

Case 6—B S, H-18-191, female, age 11, was seen in the clinic, February 14, 1935, with complaint of pain in the right ankle. She sprained her ankle two years ago, but received no treatment. Since then the ankle has been painful on exercising. She walks with a marked limp, and is unable to run. She does not believe the symptoms are increasing. Examination showed marked limp on the right. There was swelling about both malleoli, and atrophy of the calf. Tenderness to pressure was elicited below both malleoli, with a boggy feeling.

FIG 4



FIG 5

FIG 4—Case 4 Posttraumatic aseptic necrosis of the astragalus
FIG 5—Case 5 Probably osteochondroma of the astragalus

Roentgenologic examination shows a large excavation involving most of the astragalus, leaving what seems to be a thin, somewhat wrinkled cortex of bone separating the excavation from the ankle joint. The destruction extends close to the subastragalar joint, but has apparently not perforated into it. There is no reaction in the surrounding bone (Fig 6). Giant cell tumor or cyst were suggested as possible diagnoses.

The patient was admitted, and astragalectomy performed, March 15, 1935. At operation, the astragalus was found to contain a thin-walled cyst. *Pathologic Report*: Osteitis fibrosa cystica, with scattered giant cells.

FIG 6

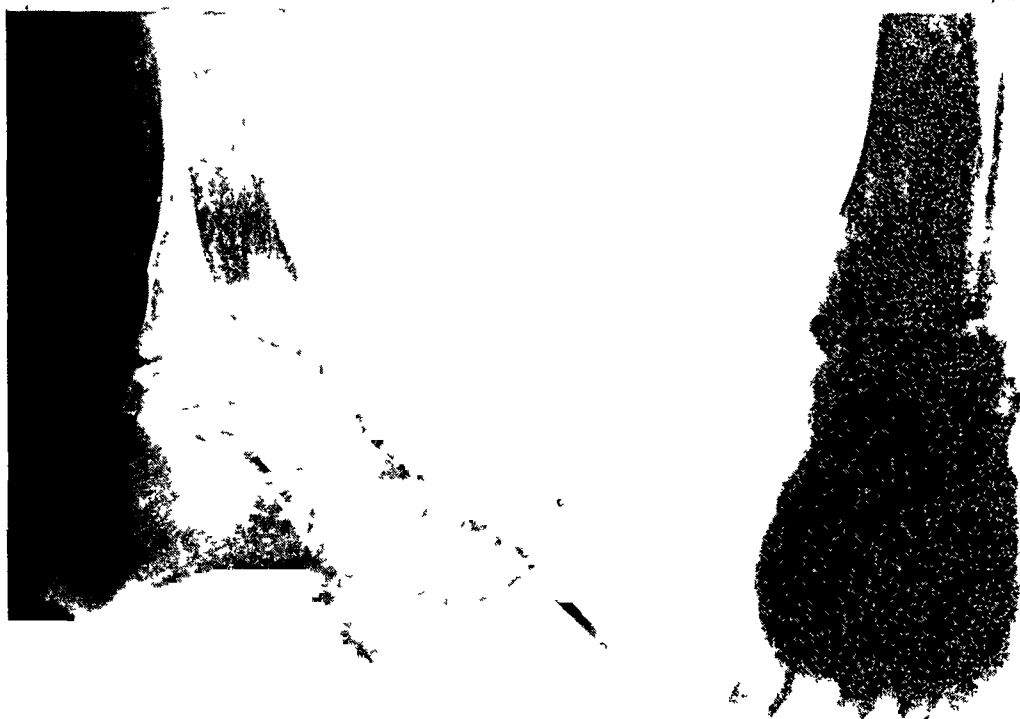


FIG 7

FIG 6—Case 6 Osteitis fibrosa cystica of the astragalus
FIG 7—Case 7 Chondromatous giant cell tumor of the astragalus

Postoperative Course This was complicated by a considerable soft tissue slough, for which skin grafting was done subsequently. She was discharged May 28, 1935, and was seen in followup as late as May, 1939, at which time conditions were generally very satisfactory.

Case 7—E W, H-34-859, male, age 20, was seen in the clinic, July 8, 1940, with a history of spraining the left ankle two years ago, with intermittent trouble



FIG 8—Case 8 Adenocarcinoma metastasis to the astragalus, probably primary in breast

ever since. The complaint was pain on walking. Examination showed moderate swelling, with tenderness at the front of the ankle joint and below the mesial malleolus.

Roentgenologic examination, July 10, 1940, showed that the body of the left astragalus seemed to consist of an irregular central cyst-like rarefaction, surrounded by quite irregular, heavily eburnated walls. There was some collapse of the upper surface of the astragalus, and there were quite pronounced evidences of secondary osteo-arthritis of the ankle joint (Fig 7). The appearance suggested a cyst which had fractured, then healed with considerable stability.

At operation, July 26, 1940, the body of the astragalus was found the site of a large cavity containing a small amount of tissue. The cavity was packed with bone chips, and an ankle fusion was performed. *Pathologic Report* Doctor De Santo and Doctor Fred Stewart. Chondromatous giant cell tumor.

The patient made a good recovery, and was seen at follow-up in September, 1941, at which time conditions were very satisfactory

Case 8—F K, H-30-602, female, age 50, was seen in the clinic in September, 1938, with a history of pain in the right ankle for three-four months. The pain was present day and night, and there was some swelling. Five years before she had had breast removed at Memorial Hospital for a tumor which she had been informed was benign. Examination showed some swelling and tenderness about the right ankle. Motion was free. Roentgenograms were reported as showing no definite pathology other than the swelling.

The patient was treated by support and conservative measures, without appreciable relief. She was finally placed in a walking plaster boot for seven weeks, with some relief. Upon removal of the boot, roentgenologic reexamination showed, in addition to generalized osteoporosis, extensive destruction in the body of the astragalus, with irregularity in the upper articular surface suggesting pathological fractures (Fig 8). A review of the previous films of four months before, showed that the destructive changes were faintly visible at that time. At orthopedic staff conference the vote was evenly divided between tuberculosis and metastatic malignant tumor.

Biopsy—January 13, 1939. Metastatic adenocarcinoma, most probably primary in breast. Roentgenologic examination of the skeletal system and chest showed areas of reduced density in the skull suggestive of metastatic lesions. No other foci were found. The patient was referred to Memorial Hospital for treatment.

SUMMARY

Eight less commonly encountered lesions of the astragalus are cited to call attention to the wide variety of pathology occurring in this bone.

POSTERIOR PITUITARY EXTRACT IN ANESTHESIOLOGY

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THE USE of posterior pituitary extract has long been common in the delivery room by the obstetrician for controlling postpartum hemorrhage and in the operating room by the surgeon for preventing postoperative intestinal atony. Few articles have been published on the use of posterior pituitary extract from the viewpoint of the anesthesiologist.¹ We have had extensive experience with this agent, primarily, because, in 1939, our attention was called to its value as an aid to greater relaxation with general anesthesia and in supporting blood pressure during spinal anesthesia. During the past two years we have used various forms of posterior pituitary extract in more than 200 abdominal, surgical, and obstetrical operations under spinal or inhalation anesthesia. We have never employed this drug routinely, but have reserved its use for only such cases in which the support of the peripheral circulation was especially important, as in high spinals in asthenic individuals, and in general and spinal anesthesia where contraction of the intestine was essential for the ease of operation, e.g., evisceration, diaphragmatic hernia, large ventral hernia, gastrectomy, biliary tract operations, abdominal perineal resection, and in genito-urinary and gynecologic procedures where some degree of intestinal atony was noted preoperatively. We have been inclined to use it more often when the surgeon was known to be a spinal enthusiast and was prone to find any inhalation anesthesia relatively unsatisfactory if the intestine was not contracted, even though the abdominal wall was relaxed and the patient was in an induced apnea. Our experience has been so favorable that we are finding more frequent indications for its use, and are herewith publishing the observations of this experience. Furthermore, we have covered the subject of posterior pituitary extract in some detail because it provides an excellent example of the correlation of facts which anesthesiologists should carry into the operating room for the practice of "internal medicine in the operating room," which is the term we have been using to describe the duties of the anesthesiologist in a surgical or obstetrical team.

PHARMACOLOGY

Posterior pituitary extract is capable of inducing pronounced physiologic changes, namely

- 1 Stimulation of the myometrium resulting in an increase in muscle tone and in amplitude of contractions, larger doses may cause uterine tetany. This oxytocic action is more evident during the last two weeks of menstrual cycle and during the later months of pregnancy, apparently as a result of the presence of an increasingly dominant concentration of estrone which intensifies the response of the uterus to any stimulant of the myometrium. Progesterone decreases the oxytocic action. In experimental animals

Newton⁶ demonstrated that only the fundus responds to pituitary extract

2 Contraction of blood vessels by direct action on the musculature of the vessels, unrelated to adrenergic nerves. The capillaries are especially constricted although there is some effect on arterioles. There sometimes follows, under general anesthesia, a rise in blood pressure which is more prolonged but less marked than that produced by epinephrine. The effect on the heart is variable, depending chiefly on a decrease in coronary blood-flow due to coronary vasoconstriction. Electrocardiographic changes, such as prolonged A-V conduction time and sino-auricular block, have been shown by Melville¹⁵ to depend upon alterations in coronary circulation. Slowing of the heart rate is a compensatory mechanism to offset the effect of peripheral vasoconstriction on the blood pressure. Anesthesia depresses this compensatory reflex sufficiently to allow a rise in blood pressure to occur in anesthetized subjects, but there is no such rise in the normal individual, in fact, a fall in systolic blood pressure occurs in the unanesthetized dog, probably as a result of coronary vasoconstriction.¹² Grollman and Geiling⁹ carefully studied the effects of the pituitary extract upon the circulation of normal man. They found no rise in blood pressure, the heart rate, oxygen consumption and cardiac output were temporarily diminished, the venous blood became arterial in character—these changes lasted about five to ten minutes and were followed by a sustained increase in cardiac output and oxygen consumption. They concluded that the cardiac and peripheral vascular effects of pituitary extract combined to interfere with the tissue supply of oxygen with a resulting accumulation of metabolites and an oxygen debt, which were then compensated by the more lasting increase in cardiac output and oxygen consumption. The vasoconstrictor activity of pituitary extract differs from that of epinephrine in two respects. (a) The former depends on direct action on vascular musculature, whereas the latter acts upon adrenergic nerve endings, and (b) epinephrine increases cardiac output while constricting the peripheral vessels so that the compensatory cardiovascular reflexes are unable to prevent a rise in blood pressure. Pituitary extract does not stimulate the heart while constricting the peripheral vessels, therefore, the systemic blood pressure is not elevated.

3 Stimulation of intestinal musculature to contraction by direct action on the muscle cells. This is produced particularly by the pressor fraction of pituitary extract which causes marked peristaltic contractions of the small intestine and colon with propulsion of the contents of the small intestine into the colon. The oxytocic principle does not add anything to the intestinal effect, it may even interfere with the maximum constriction of the small intestine by the pressor fraction because the oxytocic principle relaxes the circular muscle of the small intestine.¹⁶ Lofstrom,¹³ with an experience of 2,000 cases in which 1 cc (20 units) of pitressin was injected intramuscularly in unanesthetized subjects for the elimination of intestinal gas shadows in roentgenography, observed no effect on the stomach under any condition, none on the contracted jejunum, increased tone of the ileum, if the small intestine was inflated by stasis, paralysis or obstruction there was

a pronounced increase of tone and narrowing of the lumen, the colon almost always showed marked narrowing of the lumen, increased peristalsis and a considerable shortening of the longitudinal measurements with withdrawal of the hepatic and splenic flexures out of the upper abdominal quadrants. The pitressin action began in 5-10 minutes and was maximal in 15-30 minutes. Guthrie and Barger,¹⁰ employing a dose of 20 units of a preparation containing all the posterior pituitary principles, and using human subjects with colostomies, and reporting the activity of the terminal ileum, transverse colon and sigmoid flexure, drew the following conclusions: (a) Pituitary extract is a constant, regular and powerful stimulant of intestinal peristalsis, acting with equal strength on both the colon and the ileum, (b) it increases the motility of the intestine without exerting an effect on tonus, and (c) its action appears within 3-5 minutes and gradually decreases over a period of 45-90 minutes. The absence of an obvious tonic effect in this study, in contrast with the results of Lofstrom's work, may be explained by the presence of a colostomy in each subject, whose intestine was probably more tonic than normal before the pituitary extract was injected. Also, to be noted is the use of whole pituitary extract instead of pitressin which has a more consistent tonic effect on human intestines.^{3, 20}

4 The antidiuretic action is produced by the fraction of pituitary extract which contains the pressor principle. The site of action is probably the loop of Henle of the renal tubule, where Marshall¹⁴ has localized the site of osmotic work in the reabsorption of water. The antidiuretic substance is supposedly essential for the cells of the loop of Henle to reabsorb water to their maximal capacity but it does not increase the capacity of the tubular cells to do osmotic work. If a normal kidney is already excreting a maximally concentrated urine, the action of posterior pituitary substance is not detectable. Thus, the antidiuretic hormone will inhibit a water diuresis, but it is ineffective against a salt- or urea-induced diuresis, for the kidney is concentrating the salt or urea to its maximal ability. Not only the osmotic diuretics but also the xanthines and mercurials counteract the antidiuretic action of posterior pituitary extract. Despite the fall in volume of urine, more chloride is excreted, per unit of time, during posterior pituitary antidiuresis than previously.⁷ Antidiuresis by pituitary extract, because it does not interfere with the renal excretion of salt, urea and chloride, is safe for most surgical patients, despite the transient oliguria.

ADMINISTRATION

The official posterior pituitary preparation for injection is the solution of posterior pituitary, U S P containing approximately equal quantities of both the oxytocic and pressor principles. It is marketed in the concentration of 10 units of oxytocic activity per cc. No assay is made for pressor activity but this parallels oxytocic activity. Pituitrin is a brand of solution of posterior pituitary, U S P. So-called "surgical" and "obstetrical" pituitary solutions are only varieties of the U S P solution. They differ from each other only in that "surgical" pituitary contains 20 units per cc and "obstetrical" pituitary solution contains 10 units per cc (the same as solution of posterior

pituitary, U S P) All of these posterior pituitary solutions contain both the oxytocic and pressor substances in effective amounts Pitressin is a N N R preparation containing 20 units of pressor activity and less than one-half unit of oxytocic activity per cc Pitocin (N N R) contains 10 units of oxytocic activity and less than one-half unit of pressor activity The extracts of posterior pituitary are effective only when administered parenterally In the operating room, they are usually administered subcutaneously or intramuscularly, rarely intravenously The site of injection sometimes is the uterus, cervix, or parametrium, but these not only show no advantage over injection in the arm or thigh but are more frequently followed by "pituitrin shock "

RELATIONSHIP TO OPERATING ROOM MEDICINE

I The most common operating room use of posterior pituitary extract is as an oxytocic after the pregnant uterus has been emptied by cesarean section or vaginal delivery Some obstetricians inject the solution immediately after the presenting part has been delivered, but most await the extrusion of the placenta The usual dose is 1 cc of "obstetrical" or U S P solution, or 1 cc of pitocin injected intramuscularly The effect comes on within five minutes and lasts from 30 to 90 minutes The intra-uterine injection of pituitrin possesses no advantage over intramuscular injection elsewhere, and may even be more hazardous because of the greater likelihood of inadvertently injecting the solution intravenously in the very vascular gravid uterus Certainly, intravenous or intra-uterine injection more commonly produces "pituitrin shock"¹ For this oxytocic effect alone it would be wiser to use pitocin, which has no constrictor action on the coronary arteries, or ergonovine "Ergonovine, due to its low toxicity, rapid onset and sustained duration of action, can replace posterior pituitary extract as well as all other ergot preparations"⁸ The intramuscular or intravenous injection of a dose of 0.2 mg gives a rapid and lasting response "Pituitrin shock" is not too uncommon (1-5% in some series,¹) therefore, it is better judgment to use efficient substitutes for posterior pituitary extract when the latter is being used in a patient unprotected against its anaphylactic and coronary constrictor side-effects by ephedrine or ether anesthesia (see below)

The use of posterior pituitary extract for the contraction of the non-pregnant uterus and for capillary vasoconstriction of the genital tract to decrease operative bleeding is common among many gynecologists It is debatable how effectively capillary vasoconstriction by pituitrin decreases blood loss but some observations^{20, 3} tend to favor this belief We have not been impressed by any hemostatic or ischemic quality of pituitrin in non-obstetrical surgery

It is important to know that the occasional use of posterior pituitary extract for the induction of labor at term may require the emergency administration of general anesthesia to relax the uterus thrown into tetany even by the cautious use of the drug Ether is the anesthetic of choice here because it easily and directly relaxes the uterus and so allows the placental circulation to become adequate for the fetus

2 Solution of posterior pituitary, U S P of pitressin was first suggested by Melville¹⁷ as a means of intensifying the effect of ephedrine in supporting the blood pressure and peripheral circulation during spinal anesthesia. The combination is more effective than either drug alone. The ephedrine also prevents the coronary vasoconstriction which may result from the unopposed use of pituitary extract. The value of this combination has been confirmed by our experience and that of Hand and Sise,¹¹ and Chaikoff.⁵ We employ this pressor mixture, pituitrin or pitressin 5 units plus ephedrine sulphate 25-50 mg., as premedication for operations under spinal anesthesia when it is important to have a maximally contracted intestine or uterus or when it is likely that the blood pressure may fall severely, as in a high spinal in an asthenic patient. However, a marked elevation of blood pressure by pituitrin or pitressin alone has been reported in patients with pre-eclampsia or thyrotoxicosis. This should be regarded as a warning against the use of the pressor fraction in patients with either of these complications. The pressor and antidiuretic actions can throw a pre-eclamptic woman into eclampsia.

Posterior pituitary solution is also useful as a bowel constrictor during general anesthesia. This valuable fact is too little appreciated in anesthesia, even though it was published by Potte and Mueller,¹⁸ in 1932, and by Black,³ in 1934. The injection of the pressor fraction (5-10 units) just before or during operation under general anesthesia helps greatly in making a general anesthesia approach a spinal in the qualities which have made the latter so desirable as to be termed "the surgeon's paradise." (Similar effects have been observed when we have employed prostigmine as a bowel constrictor.) A serious and common disadvantage of even the most relaxed and quiet abdominal field under any general anesthesia is the absence of a contracted intestinal tract. Five minutes after an intramuscular injection of 5-10 units of posterior pituitary extract or pitressin one usually sees a marked narrowing of the intestine, accompanied by greater relaxation of the abdominal wall.^{3, 18, 20 *} "This effect may be very striking and seems analogous to the relaxing effect reported by Garrelon following the administration of physostigmine in cases of resistant abdominal rigidity during celiotomy."⁴ We have, therefore, found this drug especially useful in operations for evisceration, large ventral hernia and biliary tract disease under general anesthesia and even spinal anesthesia,⁵ where pre-medication with ephedrine,

* The very recently published study of Adler, Atkinson and Ivy²¹ indicates that we have been using unnecessarily large doses of posterior pituitary extract for gastro-intestinal contraction. They observed strong coordinated contractions of the colon in 28 of 31 experiments on four human subjects with a colostomy, who were injected with 1 to 2 units of surgical pituitrin intramuscularly, the effect appeared within 3 minutes and lasted 15-20 minutes. When 125 units of pituitrin was combined with 1 cc. prostigmine 1:4000, the colon contractions were increased in both degree and duration. No side-effects on heart rate, blood pressure or clinical comfort were noted. We have not yet had the opportunity of putting this mixture to the test under anesthesia. For the immediate purpose of the anesthetist however, it was gratifying to learn of their good results with 1-2 units of pituitrin alone. In recent cases we have obtained a continued bowel constriction during operation by repeating the injection of 2 units of pituitrin or pitressin every 20 minutes or as often as needed.

atropine or scopolamine may have favored intestinal relaxation. On the other hand, the pressor extract should be avoided where intestinal perforation or obstruction is present or suspected.

The prevention of postoperative distention with posterior pituitary extract may well be started in the operating room^{3, 18, 19, 20} in any case, but especially if there is a marked likelihood of such a complication, e.g., extensive handling of intestine, or when it is important to prevent it, e.g., extensive ventral herniorrhaphy, or celiotomy in a cachectic patient.

3 A desirable side-effect of the operating room use of pituitary extract or pitressin is retention of water induced by the antidiuretic fraction. The surgical patient without heart failure, epilepsy, pre-eclampsia or nitrogen retention is greatly aided in maintaining water balance by any measure which reduces water loss during the important period immediately following operation or delivery, when water intake is negligible unless administered parenterally. Postoperative dehydration has been observed to be greatly decreased by the use of pitressin²⁰.

4 The treatment of shock due to decreased blood volume by the use of posterior pituitary extract is ineffective and illogical, it may even be dangerous because of its coronary vasoconstrictor action (see Case 1 of Buist⁴). But shock of neurogenic origin, as that caused by a celiac plexus stimulus during upper abdominal surgery or by spinal anesthetic relaxation of muscles, arterioles and veins, is successfully and logically prevented or treated by the pressor fraction of posterior pituitary solution, alone or, better yet, combined with ephedrine to intensify the pressor action and antagonize the coronary vasoconstriction.

The use of pituitrin is very frequently followed by a marked pallor of the skin, especially of the face, because of intense capillary vasoconstriction, it may appear alarming but it is not dangerous and requires no treatment. It may, if so desired, be promptly replaced by a pink flush by the subcutaneous injection of 3-5 cc coramine, which has the nictinic acid property of dilating the skin capillaries, especially those of the face. A less common but more serious effect of pituitrin is a marked drop in blood pressure. In some cases this has been due to allergy,^{1, 2} and in other cases, to coronary artery constriction^{1, 4}. The treatment of "pituitrin shock," of either origin, is the administration of a high oxygen concentration and the intravenous injection of 0.1 cc of ephedrine or epinephrine (or if the patient is under cyclopropane anesthesia, 0.1 cc neosynephrine). Pituitrin or pitressin should not be used in a patient with hypertension or coronary artery disease because it may induce a dangerous degree of coronary artery insufficiency^{4, 19}.

* Another very recent study is mentioned here because it provides further confirmation of the fact which we have repeatedly observed clinically, in our use of pituitrin under all forms of anesthesia except cyclopropane, namely, that small doses of pituitrin or pitressin have a large margin of safety. Graybiel and Glendy²² demonstrated, using a slow infusion of a 1:1000 dilution of pitressin in nine normal persons, four patients with essential hypertension, and two patients with angina pectoris, that marked gastro-intestinal contraction could be produced in every case with no, or slight changes in blood pressure, pulse rate, cardiac output and without any change

In such a patient under cyclopropane-ether anesthesia, three units of pituitrin, by hypodermic, has started a series of marked cardiac arrhythmias, ranging from slow coupled beats to a rapid "irregular irregularity" like that of auricular fibrillation, accompanied by a sharp, marked rise of blood pressure from 140/90 to 220/110. This disappeared in a half hour, fortunately, leaving no ill-effect. This experience has not been tested by repetition, but it may indicate that the pressor extract and cyclopropane are incompatible because of a synergistic tendency toward the production of hypertension and/or cardiac arrhythmias.

5 The pressor fraction of pituitary extract can produce a parasympathicomimetic stimulation of the respiratory tract,⁴ which is always undesirable during anesthesia. Within five to ten minutes after injection, the respiration of the patient may show a laryngospasm ("crowing") or bronchoconstriction (asthmatic wheezing) or bronchorrhea. Any or all of these untoward signs are favored by an asthmatic predisposition or by cyclopropane, which is also parasympathicomimetic. We have rarely seen any of these respiratory complications in our use of pituitary extract, they have not been noted by others who injected this drug during general anesthesia with avertin-nitrous oxide-oxygen¹⁸ or ether.^{3,20} We have rarely employed it while administering cyclopropane alone, and never used it in an asthmatic patient. Wylie,²⁰ too, has found cyclopropane anesthesia to be incompatible with pituitary extract. If pituitrin has been urgently needed for its effect on the intestine during cyclopropane anesthesia, we have added ether. Burstein, however, has reported several such instances of pituitrin-induced respiratory complications during and after anesthesia. We prevent these by avoiding the use of the pressor fraction during cyclopropane anesthesia, i.e., use pitocin if only the oxytocic effect is desired, when the pressor fraction is required to contract the bowel during cyclopropane anesthesia, we add ether. The treatment of these respiratory complications during general anesthesia is the injection of ephedrine or the inhalation of ether-oxygen anesthesia, with the addition of helium if the tidal respiratory volume is greatly reduced by the broncho-constriction or laryngospasm. We have not required the aid of ephedrine or helium in any of our few instances of mild laryngospasm.

CONCLUSIONS

Posterior pituitary preparations can be more frequently used to advantage in the operating room than has been the custom in the past. They

in the normal electrocardiogram or cardiac symptoms. If the coronary arteries were constricted by these doses, which produced bowel activity, then the decrease in coronary blood flow was compensated for by the decrease in the work of the heart resulting from the 10.8 per cent drop in average metabolic rate and the 5 per cent decrease in average cardiac output. "Pitressin in amounts sufficient to provoke distressing abdominal cramps does not significantly decrease the blood supply to the myocardium in relation to the work of the heart and it is safe and practical to give pitressin to patients with coronary heart disease." Certainly the intramuscular administration of the 1-2 units of pituitrin or pitressin, found to be effective on the colon by Adler, *et al.*,²¹ is safe, even for cardiac patients, for the doses employed by Graybiel and Glendy²² were much greater, and were given by vein.

aid both the anesthetist and the surgeon, and, therefore, serve in the best interests of the patient. By their judicious use, we can secure a more stable peripheral circulatory system, a more relaxed abdominal field, better hydration, less blood loss, more expeditious and less traumatic surgery, and a decreased likelihood of postoperative intestinal atony. As with all potent drugs, the avoidance of untoward reactions requires individualization of patients and a detailed knowledge of drug behavior and their antagonists.

REFERENCES

- ¹ Adelman, M. H., and Lennon, B. B. Pituitrin Shock. *Amer J Obst & Gynec*, **41**, 652-659, 1941
- ² Bickers, Wm. Shock from Posterior Pituitary Extract. *South M J*, **34**, 1112, 1941
- ³ Black, C. V. Pitressin in Surgery. *Jour Kans Med Soc*, **35**, 216, 1934
- ⁴ Burstein, C. L. Clinical Observations on some Systemic Effects of Pitressin. *Amer J Surg*, **ns**, **52**, 455, 1941
- ⁵ Chaikoff, J. S. Efficacy of the Combination of Ephedrine and Pitressin as Pre-Anesthetic Medication in the Control of Blood Pressure during Spinal Anesthesia. *Curr Res Anesth and Analges*, **19**, 121, 1940
- ⁶ Goodman, L., and Gilman, A. *The Pharmacological Basis of Therapeutics*. Macmillan Co., N. Y., 1941, p. 662
- ⁷ *Idem ibid*, p. 684
- ⁸ *Idem ibid*, p. 669
- ⁹ Grollman, A., and Geiling, E. M. K. Cardiovascular and Metabolic Reactions of Man to Intramuscular Injection of Posterior Pituitary Liquid (Pituitrin), Pitressin and Pitocin. *J Pharmacol & Exper Therap*, **46**, 447-460, 1932
- ¹⁰ Guthrie, J. S., and Barger, J. A. The Effects of Drugs on Different Segments of the Intestine of Man. *Surg, Gynec & Obst*, **63**, 743-749, 1936
- ¹¹ Hand, L. V., and Sise, L. F. *Surg, Gynec & Obst*, **71**, 9, 1940
- ¹² Kolls, A. C., and Geiling, E. M. K. Pharmacology of Extracts of Posterior Lobe of Pituitary Gland. *J Pharmacol & Exper Therap*, **24**, 67-81, 1924
- ¹³ Lofstrom, J. E. Further Observations on Elimination of Intestinal Gas Shadows in Roentgenography. *Radiology*, **36**, 34, 1941
- ¹⁴ Marshall, E. K., Harvey, A. M., and Buigess, W. W. Site of Antidiuretic Action of Pituitary Extract. *J Pharmacol & Exper Therap*, **49**, 237, 1933
- ¹⁵ Melville, K. I. Electrographic and Blood Pressure Changes Induced by Posterior Pituitary Extract and Influence of Ephedrine thereupon. *J Pharmacol & Exper Therap*, **64**, 86-110, 1938
- ¹⁶ Melville, K. I., and Stehle, R. L. Actions of Pituitary Preparations (Posterior Lobe) upon Intestines of Dog. *J Pharmacol & Exper Therap*, **50**, 165-173, 1934
- ¹⁷ Melville, K. I. Combined Ephedrine-Pituitary Extract Therapy in Histamine Shock. *J Pharmacol & Exper Therap*, **44**, 279, 1932
- ¹⁸ Potter, P. C., and Mueller, R. S. Posterior Pituitary Extract in Prevention of Post-operative Intestinal Disturbances. *ANNALS OF SURGERY*, **96**, 364, 1932
- ¹⁹ Seed, L., Falls, F. H., and Fantus, B. Pitressin in Laparotomies. *Surg, Gynec & Obst*, **64**, 895-905, 1937
- ²⁰ Wylie, L. A. The Use of Pitressin in Preoperative and Postoperative Treatment. *Jour Florida Med Ass'n*, **28**, 229, 1941
- ²¹ Adler, H. F., Atkinson, A. J., and Ivy, A. C. Supplementary and Synergistic Action of Stimulating Drugs on the Motility of the Human Colon. *Surg, Gynec & Obst*, **74**, 809, 1942
- ²² Graybiel, A., and Glendy, R. E. Circulatory Effects following the Intravenous Administration of Pitressin in Normal Persons and in Patients with Hypertension and Angina Pectoris. *Am Heart J*, **21**, 481, 1941

REGIONAL ILEITIS*

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TEN YEARS AGO an article was published from the Surgical and Pathological Services of the Mount Sinai Hospital, which served to clarify the pathologic, clinical and surgical features of the disease process termed regional ileitis. We feel that, after a decade, a review of our experiences with the disease at this institution may prove of considerable interest.

The question may be raised whether regional ileitis is essentially a surgical disease. Our experience leads us to believe that it is. A great deal of the confusion surrounding this issue arises from the failure to differentiate between the localized form of the disease, which is confined to the distal four or five feet of ileum, and the more generalized type, in which the distal involvement is only part of a generalized enteritis of various extent and degree. For this reason we consider the term regional ileitis a poor one and believe that the term "distal ileitis" should be reserved for that variety of the disease amenable to surgical treatment.

In the original paper on the subject, the importance of limiting surgical consideration of the disease to the distal type was emphasized. Unfortunately, numerous publications which emphasized what was already known, namely, that proximal segments might also be involved, served to obscure the issue. With increasing experience, we have learned that so-called jejuno-ileitis is much more common than we at first appreciated. Therefore, at the present time, in addition to a careful preoperative roentgenologic study of the entire small bowel, a painstaking exploration of the small intestine is carried out before definitive surgical therapy is undertaken. Our experience with 77 operatively proven cases seems sufficient evidence that distal ileitis confined to the distal segment is a clear-cut disease entity. Some of these patients have been followed for many years without demonstrating recurrent or new lesions. During the same period, 22 cases of jejuno-ileitis, of whom eight were verified by operation, were encountered. This group was reported by Wachtel and Sussman. We cannot emphasize sufficiently the necessity of demonstrating that one is dealing with the localized form of the disease. In the diffuse variety, there may be many feet of apparently normal bowel between the upper and lower diseased segments. The importance of a careful examination of the entire small bowel at operation becomes apparent. In many cases the disease extends so high into the proximal small bowel that any short-circuiting or resection procedure will result in severe nutritional disturbances incompatible with life. We have reached the opinion, therefore, that jejuno-ileitis is a nonsurgical disease.

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Another disease which may closely simulate regional ileitis is regional or migratory colitis, a localized right-sided colitis of the type described by Bargen and Weber. In many of these cases the distal 12 inches, rarely more, of the terminal ileum may be involved. Curiously enough, this lesion may be detected roentgenologically more easily than the concomitant more important colonic lesion. Exploration is often difficult because of the inability of the surgeon to deliver the cecum and ascending colon into the wound for close inspection. Very often, only the surgeon with considerable experience can detect the inflammatory changes in the wall of the right colon in this disease.

Another question which is frequently asked is whether resection of the diseased segment of bowel is always necessary. It is our belief, based upon a fairly extensive experience, that such radical treatment is rarely indicated. This view has been stressed in previous communications. At Mount Sinai Hospital our experience has convinced us that ileocolostomy *with exclusion* will prove effective in the vast majority of cases. We adopted this procedure quite by accident, after noting the marked improvement which followed the operation when it was performed as the first step of a contemplated two-stage procedure.

Our reasons for adopting ileocolostomy *with exclusion* as the operation of choice in the treatment of distal ileitis may be briefly stated as follows.

In eight instances, secondary exploration, or resection, revealed healing in the previously diseased excluded loop of bowel. In one instance, autopsy, after death due to other causes four years later, showed complete healing. In seven cases, discharging fecal fistulae closed spontaneously following this operation. In the remaining cases, clinical improvement, as manifested by disappearance of inflammatory masses, subsidence of prolonged fever, disappearance of intestinal symptoms, gain in weight and nutrition, and disappearance of anemia, were so marked as to render inescapable the conclusion that amelioration or healing of the pathologic process had occurred.

TABLE I
ILEITIS CASES—Total 77

<i>Ileocolostomy with Exclusion</i>	54 cases	<i>Ileocolic Resections</i>	23 cases
Mortality	0	Deaths	4
<i>Persistence of Disease in Excluded Loop</i>	5 cases	<i>Proximal Involvement</i>	3 cases
3 yrs postop 1 well 3 years after resection		One of these died of malnutrition and exhaustion	
1 yr postop 1 well 1 year after resection		Multiple operations	No
Less than 1 year 3—2 died of continued sepsis 1 well after resection		ileitis at autopsy	
<i>New areas of Involvement</i>	2 cases		
Both within 1 year			

An important point in favor of this operation is its low mortality. To date, 54 such operations have been performed without a death. If recession of the disease in the excluded loop of bowel does not take place, the secondary resection carries with it less risk. In these 54 cases, the disease failed to recede in five instances. Two of these patients had associated ileocecal fistulae, and both died of persistent sepsis, probably due to progressive retro-

peritoneal infection In two instances, following the short-circuiting operation, new areas of involvement appeared proximal to the site of anastomosis In addition, two relatively minor complications have been encountered In one case, intussusception of the excluded loop into the cecum took place Dr Slocum, who was kind enough to furnish us with the essential details, operated upon this patient at the Monmouth Memorial Hospital It is interesting to note that, in this instance, there was extensive recession of the disease process to permit of intussusception which could not have occurred if the loop of the bowel were still rigid, thickened and narrowed In one other case, there was transient melena unaccompanied by other symptoms, which occurred about four year after operation It persisted for one week and stopped spontaneously

It is important to clarify the cause of the symptom of postoperative diarrhea, because it has been frequently stated that the continuation of diarrhea is indicative of persistence of the original disease Our experience has been quite the opposite of this view This painless and otherwise symptomless diarrhea is frequently encountered during the first few months following the exclusion and short-circuiting operation In some patients it has persisted for longer periods On two occasions it resulted in the performance of exploratory celiotomy, which revealed, in each instance, no evidence of disease It must be remembered that this operation is not exactly similar to that performed for carcinoma of the right colon In the latter, the resection is rarely carried more than six or eight inches proximal to the ileocecal junction In distal ileitis, the anastomosis is not infrequently made four to five feet from the ileocecal angle The entrance of the more fluid intestinal contents from this higher segment of small bowel is probably more irritating to the colon than when the anastomosis is made at a lower level We believe that this is the logical explanation of this symptom, and that the period of time that it persists will depend on the length of ileum excluded and the rapidity of readjustment of the remaining ileum to the function of water absorption

In 23 instances, ileocolic resection was performed There were three deaths In three cases, the disease reappeared postoperatively in the bowel proximal to the anastomosis It is probable that "skip-areas" were overlooked at the first operation Two patients were subjected to three operations One of these died six years following the first operation It was thought that ileitis and colitis had developed, but autopsy failed to corroborate this diagnosis One of the other patients died four years postoperatively from intestinal obstruction due to a band In this instance, also, there was no evidence of any further disease While it is true that in the uncomplicated case and in the hands of an experienced surgeon, resection can also be carried out with a low mortality rate, it is important to remember that, in the more complicated cases with fixation to adjacent viscera or in the hands of a less experienced surgeon, it would be extremely difficult to keep the

mortality figures as low as those attending the simpler short-circuiting procedure

The belief that it is necessary to resect widely the mesentery of the involved segment of bowel because of the danger of retrograde spread *via* the lymphatics seems to us to be unfounded. In the first place, secondary operation has, on a number of occasions, disclosed complete recession of previously enlarged and edematous nodes to normal size and consistency. Secondly, many of these patients have had the disease for years before operation without any spread to more proximal segments. And, finally, such extension has occurred even after the widest type of resection.

The clinical picture of distal ileitis is more easily interpreted when the underlying pathologic lesion is clearly understood. Basically, the symptoms are of two general types. In the first, the ulcerative changes are limited to the bowel itself and produce the symptoms of enteritis and, later, those of obstruction. In these cases, the attention of the surgeon is at once directed to the intestinal tract. In the second group, the symptoms are due to the effects produced by the slow perforation of the intestinal ulcers, to the extent that the symptoms of inflammation of adjacent viscera or of the peritoneum may completely obscure the underlying intestinal lesion. The most common picture thus produced is that of local peritoneal inflammation usually in the right lower quadrant simulating appendicitis or the development of intra-abdominal abscesses. External drainage of these abscesses frequently results in the formation of chronic fistulae due to the persistence of the disease in the involved segment of bowel. Inflammatory fixation of the diseased small bowel to adjacent viscera, with or without the formation of communicating fistulae, may produce symptoms of a urologic or gynecologic nature. Perforation into the mesentery, which is quite common because of the location of the ulcerative process on the mesenteric side of the bowel, may give rise to a puzzling clinical picture, with persistent fever as the prominent symptom, especially if the process remains localized. The infection may spread widely into the mesentery and give rise, as in two of our cases, to a most extensive retroperitoneal cellulitis. Not infrequently, the fixation to adjacent viscera may produce symptoms which closely simulate primary urologic disease, and even produce roentgenographic changes in the ureter and kidney pelvis. The urologist should remember that a persistent urologic symptom, without demonstrable disease in the genito-urinary tract, may be caused by perivesical inflammation due to fixation of a diseased loop of ileum. The mechanism in these cases is similar to that which occurs in sigmoid diverticulitis. In two of our cases there occurred a perforation into the bladder and the formation of ileovesical fistulae. The efficacy of the recommended short-circuiting operation *with exclusion* was amply demonstrated when these fistulae closed spontaneously during the early days of convalescence.

The gynecologist should also remember that a loop of diseased bowel may prolapse into the pelvis, become adherent to the adnexa or uterus or

the bottom of the cul-de-sac, and produce symptoms which simulate closely primary pelvic inflammatory disease. A frequent complication is the development of multiple perianal fistulae. Penner and Crohn have described these fistulae in considerable detail, and believe that they are directly continuous with the diseased bowel by retroperitoneal extension. Our operative experience would lead us to conclude that this mechanism accounts for a very small proportion of such cases. The majority are probably due to crypt infection resulting from the long-standing foul diarrhea. From a practical standpoint, it is important to remember that fistulae which recur in spite of adequate operative intervention, in patients in whom there is no evidence of colitis or proctitis, may be due to an underlying ileitis. In a number of our cases, rectal incontinence has followed ill-advised radical operations by proctologists who failed to suspect the underlying cause of the fistulae.

The question is frequently asked what procedure should be carried out when the surgeon finds a distal ileitis during the course of an operation for supposed acute appendicitis. It is our opinion that, if an acute ileitis without perforation is found, nothing should be done. It is debatable if even appendicectomy is advisable. It is impossible to predict what the outcome in such cases will be. In a number of instances, there have been no further symptoms, and the patients are apparently well, some of them for as long as ten years. In two instances, recurrence of symptoms within a year necessitated operative intervention. With increasing experience, we have become impressed with the tendency for spontaneous remission not only in the acute cases, but in many patients with extensive involvement of ileum and jejunum which are not amenable to surgical therapy. These remissions and exacerbations are of uncertain duration and frequency. We have not as yet encountered a case of chronic distal ileitis in which such remission has lasted for a number of years.

We are frequently asked about the management of cases with fecal fistulae. There seems to be considerable misinterpretation of the exact pathogenesis of these fistulae. The belief seems to be widely held that they are due to the "blowing-out" of the stump following the appendicectomy which is frequently performed. It is possible that, as a result of the pericecal inflammation, secondary dehiscence of such a stump may occur, but this is not the primary cause of the fecal fistula. The essential factor is the perforation of one of the enteric ulcers. As the perforation frequently takes place into the mesentery, the course of the tract could be quite tortuous. Attempts at local repair are doomed to failure because of the lack of healing power in the diseased bowel. On the other hand, many surgeons believe that resection is necessary to achieve a cure. Inasmuch as this variety of the disease offers the greatest technical difficulties for the surgeon, complications are more frequent, and the mortality rate is higher. We have found the short-circuiting operation *with exclusion* most satisfactory in this type of case. In only one out of eight instances was there failure of closure of a fecal fistula. In one patient, there were so many fistulae in the lower abdomen that a

supra-umbilical transverse incision was necessary. All the fistulae closed spontaneously.

We would like to emphasize the following features in arriving at a clinical diagnosis of distal ileitis. Distal ileitis should be considered if there are persistent fecal fistulae following the drainage of so-called appendiceal abscesses. The diagnosis should be considered if, following appendicectomy, there develops a residual abscess at a later period. It should be thought of in cases of persistent diarrhea without the presence of blood in the stools. It should be thought of whenever there are intestinal symptoms, accompanied by persistent fever and the development of anemia. It should be considered when there are obscure perivesical and adnexal inflammatory conditions without demonstrable cause in the genito-urinary system. It should be thought of in the presence of persistent, multiple and intractable perianal fistulae. The clinical diagnosis can usually be confirmed by roentgenologic examination. The barium enema may delineate the diseased, string-like terminal ileum by retrograde passage of the barium mixture through an incompetent ileocecal valve.

In the operative management, the following features should be stressed:

- 1 The surgeon must be certain that he is dealing with the localized form of the disease. This requires careful inspection of the entire small intestine.

- 2 The bowel should be divided a good distance proximal to the diseased segment. It is important to look for the so-called "skip" lesions.

- 3 We recommend ileotransverse colostomy *with exclusion*, as a definitive surgical procedure. This should be performed through a left rectus incision, with the patient in Trendelenburg position. Visualization of the various bowel segments is greatly simplified by this maneuver. If resection becomes necessary at a later date, it can be carried out through a right-sided incision in a field devoid of the adhesions which result from the first operation. We wish to stress this point in technique.

- 4 When resection is performed, it is not, in our opinion, necessary to extend it to the transverse colon, as is the case with carcinoma of the right colon. Resection at the level of the ascending colon is all that is necessary.

- 5 We believe that side-to-side ileocolostomy is the safest type of anastomosis.

- 6 We urge the preoperative use of the Miller-Abbott tube, to serve both as a bowel decompressing agent and as a method of rapid orientation in cases where extensive adhesions render intestinal topography difficult to visualize.

A final word as to prognosis is in order. In our experience, extension or recurrence of the disease will manifest itself within the first two years. Of the 54 cases in which the short-circuiting operation was performed, the seven failures occurred within that period. Similarly, in the group of 23 patients subjected to resection, the three failures occurred within the same period. There were three deaths in patients in whom neither a short-circuit-

ing procedure nor a resection could be carried out. Two of these were due to extensive retroperitoneal infection, and one to a perforation of an abscess into the free peritoneal cavity. A severe colitis developed in one patient in whom a resection had previously been performed. In another patient, a universal enterocolitis developed after resection of an extensive segment of bowel high in the ileum. It is probable that the jejunum was involved at the time of the first operation. In the light of our present experience, this patient would not be subjected to operation.

On the basis of the experiences related in this communication, it is our conviction that distal ileitis is a surgical disease and that, in the great majority of cases, marked amelioration of symptoms may be obtained by the simpler operation of ileocolostomy *with exclusion*, which, so far, has been attended by no mortality.

THE INCREASING USEFULNESS OF THE DEVINE COLOSTOMY IN LEFT COLON AND RECTAL SURGERY*

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A PRACTICAL AND EFFECTIVE COLOSTOMY should possess the following essential features (1) It should permit the complete evacuation of all of the contents of the colon proximal to its office (2) It should prevent "spilling-over" of any fecal material from the proximal into the distal loop (3) It should be continent, and, by means of a small exit office, retain the major portion of the fluid contents of the colon and permit one or two natural, or by irrigation daily, bowel movements of semisolid consistency (4) It should be without skin excoriation or infection (5) It should be controlled easily by a simple occlusive pressure dressing, without the need for any bags or complicated apparatus All of these conditions are obtained by a Devine colostomy

OPERATIVE TECHNIC

The technical execution of a Devine colostomy is simple, without shock, and readily accomplished under local infiltration anesthesia There are, however, certain special details that must be observed if a good functional colostomy is to be obtained It may be placed practically anywhere throughout the colon, but meets its best indication for surgical conditions distal to the midpoint of the transverse colon The usual elective site for a Devine colostomy is midway between the hepatic flexure and the middle of the transverse colon An incision 10 cm in length is made through the upper right rectus muscle at about the middle third of the distance between the costal margin and the level of the navel The incision is carried directly through the fascia and the muscles, to the peritoneal cavity A gloved hand, coated with sterile vaseline to facilitate its introduction through the relatively short incision, is introduced into the abdomen for palpatory exploration of the abdominal viscera The contents of the upper peritoneal cavity may be visualized but the viscera of the lower portion of the abdomen must be appraised by palpation The examination should include all the abdominal viscera The surgical lesion should be accurately determined as to site, fixation, associated inflammation, the relative degree of obstruction, the amount and extent of any intestinal adhesions, and the presence or absence of lymph node and liver metastases

After the completion of the exploration of the abdomen the transverse colon is brought out through the wound, a tape is passed through the two layers of the gastrocolic omentum beneath the bowel, and used for traction

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The gastrocolic omentum and the omentum proper are dissected free from the colon for a distance of about 10 cm on both sides of the traction tape. By pulling the traction tape upwards both the afferent and efferent loops of colon fall, quite naturally, parallel to one another, producing the familiar "double-barrel shotgun" appearance. About six centimeters from the tape downward is left as a free hiatus between the two loops.

Ordinarily, it is wise to exceed the six centimeters but never less, as these free loops must later traverse the abdominal parietes without the slightest degree of tension. This feature of the technic is of great importance in the after-care and postoperative condition of the colostomy. Below the lowermost limit of the free space the two bowel loops—afferent and efferent—are approximated for at least 10 cm by suturing the inferior "white bands" together. It is preferable to add an additional second line of sutures. The next step consists of two incisions, not larger than three centimeters, made on either side of the primary longitudinal incision. The secondary incisions are made laterally about three centimeters from the skin edge of the abdominal incision and parallel to it. They should be placed so as to correspond to the middle third of the first abdominal incision. The lateral incisions divide only the skin and subcutaneous tissue. From each lateral incision a tunnel is formed toward the median incision by pushing a closed hemostat through the intervening subcutaneous tissue. Under no circumstances should the tunnel traverse any tissue except the subcutaneous fat. Through each lateral incision a six-inch crushing clamp is inserted and brought out in the area of the original incision. By gentle manipulation the two clamps are applied to the colon through the free space traversed by the tape. The bowel is divided with the actual cautery and all bowel material between the clamps burned away. By gentle maneuvering the clamps are withdrawn, with the attached bowel ends through the lateral incision—the afferent loop through the lateral incision on the patient's right side, and the efferent loop through the lateral incision on the patient's left side. The free loops of bowel should extend at least two centimeters above the level of the skin and rest easily, without tension, on the surface of the abdomen. If the lateral incisions are short, not more than three centimeters in length, the skin orifice will fit snugly, but not tightly, about the bowel tubes, and sutures will not be required. The abdominal incision is closed by interrupted through-and-through sutures of Malin stainless steel wire. This wire ties almost as readily as linen without breaking, and the sutures are always buried beneath the skin, never do they pass through the skin as ordinary retention sutures.

It is our custom to approximate the skin with Michel's clips and to put a short, five-centimeter, latex drain in the lower angle of the wound. Finally, the operative area and the bowel loops are smeared with sterile vaseline, the crushing clamps anchored to the abdominal wall by adhesive, and sterile dry dressings applied. The clamps are left on three days, occasionally they may be removed sooner, and, rarely, a Paul's colostomy tube is affixed

PLATE I

H. M. P. J. du sch

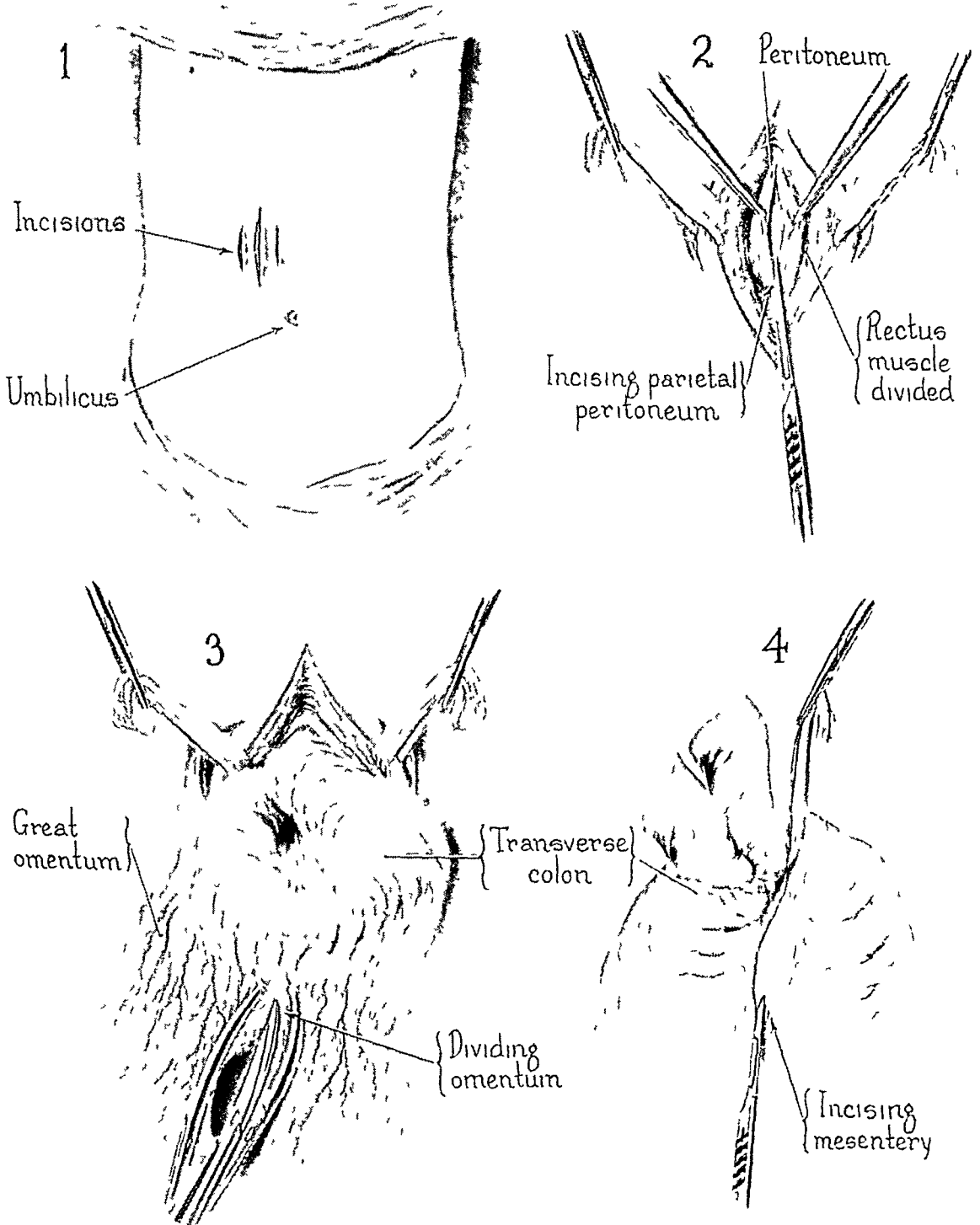


FIG 1 —Relative position of the incisions
 FIG 2 —Undermining skin with gauze retraction
 FIG 3 —Dividing the great omentum to permit eversion of colon
 FIG 4 —Tape introduced through open space to produce "double barreled colon"

W. P. Didusch

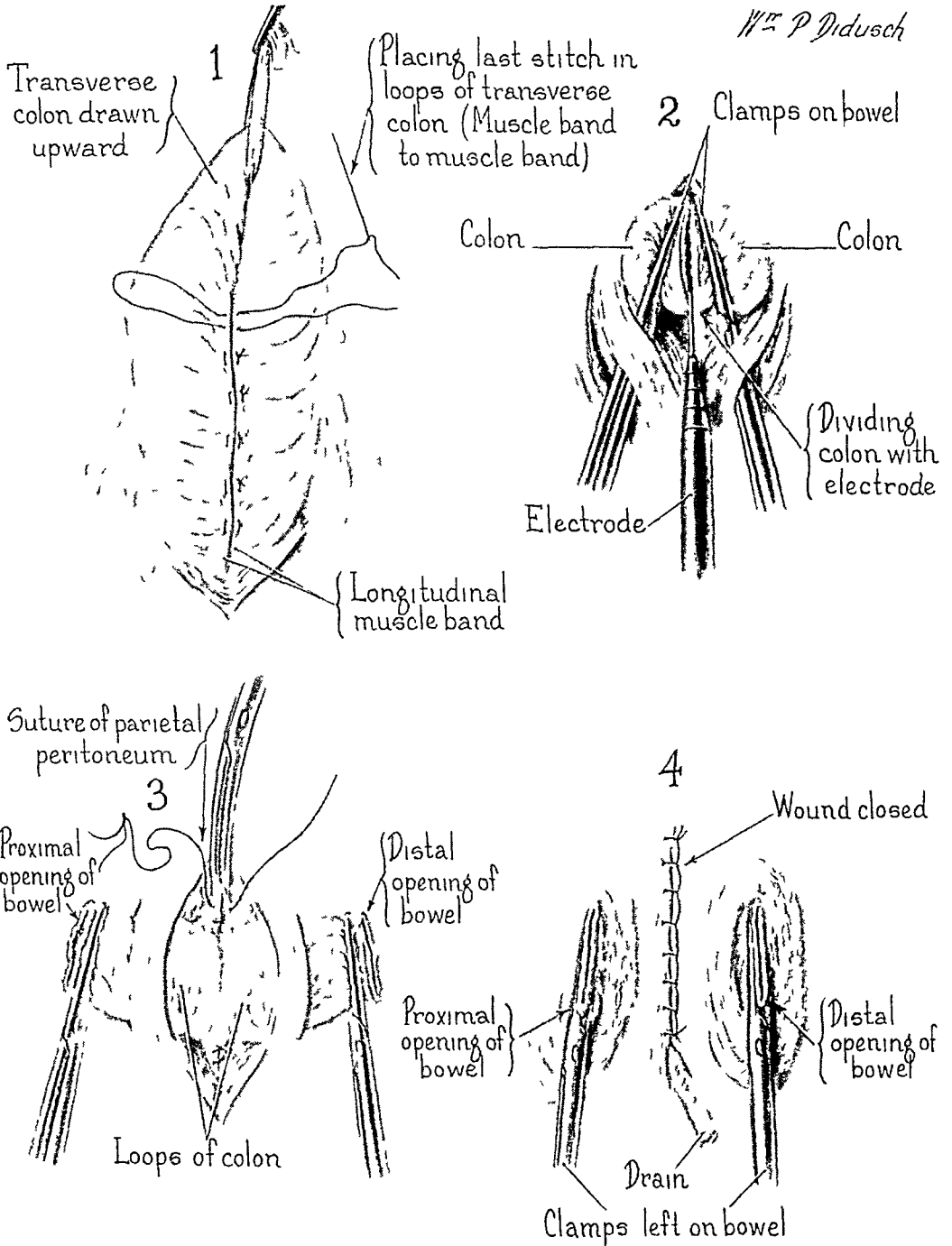


FIG. 1—Approximation of white bands by sutures.
 FIG. 2—Bowel segments clamped and colon divided by cautery.
 FIG. 3—Exit of the proximal and distal loops.
 FIG. 4—Final appearance of wounds of a Devine colostomy.

to the right afferent loop at the completion of the operation. The latex drain is usually withdrawn at the time the clamps are removed.

POSTOPERATIVE CARE

The postoperative care is simple. For 24 hours the patient receives all his fluids intravenously. Three infusions of 1,000 cc are given during the first day. The first is of normal saline, plus five per cent dextrose, the second and third are of distilled water plus five per cent dextrose. In the debilitated, anemic, or aged, or when vomiting has been present before operation, it has been our practice to add 10 cc of a 1-1,500 sterile solution of hydrochloric acid to one of the infusions of distilled water.

At the end of 24 hours the patient is given water by mouth, and as the oral intake increases the intravenous fluid is diminished *pari passu*. At the end of 48 hours soft diet may be instituted, and after the clamps are removed a gradual return to full, high protein, high caloric diet is resumed. The patient is allowed out of bed at the end of one week and may be discharged at the end of 10 days.

TECHNIC OF CLOSURE OF THE DEVINE COLOSTOMY

The closure of a Devine colostomy embraces two phases. Recently into the hospital for the application of the spur clamp, and subsequent office treatments. With the patient in the hospital, and in bed, the special Devine colostomy spur clamp, (or the Ochsner-DeBakey modification, which I personally prefer) is manipulated into place and the compression screw turned up about halfway. There is a slight degree of pain while the clamp is being applied and the compression screw turned. This discomfort lasts a few hours, and only rarely will the patient vomit from a peritoneal reflex. It is a good plan to have the head and thorax of the patient slightly raised by two pillows, or a Fowler position of 20 degrees. By this degree of elevation the small intestines fall away from beneath the colon. I do not know of any case where the application of the Devine spur colostomy "caught" the small intestine. If the double-barrelled tube of colon was adequately and properly prepared at the colostomy operation this complication should never occur.

After the clamp has been in place for 24 hours full compression is exerted by turning the compression screw up to the "hilt". In another 24 to 48 hours, a linear line, about five to six centimeters in length, will be cut through between the afferent and efferent loops. After removal of the clamp, it has been our practice to insert the index finger of each hand through the, respective, right and left colostomy orifices and "iron-out" the linear cut to a full, round, circular lumen. After this the patient may be discharged.

Normal bowel movements begin to occur *per via naturalis*. After the re-establishment of bowel movements the orifices of the colostomy begin to close by themselves. At the first visit to the office, all redundant mucous membrane is burned away with the electric cautery. If care is exercised

to cauterize only the mucous membrane no pain is experienced, although the area may get a little "hot." A short wait will allow one to proceed. With three or four cauterizations the skin covers the orifices, although gas may come through for three or four weeks on straining. After about five or six weeks the orifices remain permanently closed.

INDICATIONS FOR EXTENSION OF EMPLOYMENT OF THE DEVINE COLOSTOMY

This communication concerns itself with an extension of the indications for employing the Devine colostomy for surgical conditions of the left or distal colon.

There are certain basic or fundamental principles that underlie the acceptance of the Devine technic for colostomy in large bowel surgery. It is axiomatic that the simplest type of colostomy—that performed by mobilizing a loop of colon, transfixing it with a glass rod, and later dividing the bowel—is the worst type for function and for subsequent closure. It is of prime importance that there should be no spilling-over of feces from the proximal loop into the distal loop. Even when the bowel is completely divided in the loop colostomy a fluid stool will inevitably spill-over into the lower loop. In the Devine colostomy this is impossible, as the orifices of the two loops are separated by five centimeters of normal skin.

"If a segment of bowel is completely isolated experimentally and thus deprived of its functions, in the process of time it will lose much of its bacterial content" (Devine). It is the complete "defunctionalization and debacterialization" of the distal colon that is the outstanding feature of the Devine colostomy. Furthermore, the orifices of the colostomy, situated high up on the upper abdomen, far away from the surgical condition of the left colon or rectum, permits readily the local treatment of the entire loop of distal bowel by irrigation, instillation of solutions of the "sulfa" drugs and, more important, complete physiologic rest to the loop of bowel proximal to the surgical lesion.

In neoplasms of the left colon, sigmoid and rectosigmoid there is a constant and inherent tendency for some degree of obstruction to the bowel lumen—colicky pain and distention. Whenever obstruction begins to operate in an intestinal tube, the proximal bowel immediately responds by hypertrophy. This hypertrophy, for a variable time, is sufficient to overcome the obstruction. Later, the proximal bowel fails to keep pace with the obstruction, edema of the muscular layers takes place, and in some degree—greater or less—dilatation follows. It is not without interest that about three per cent of patients with a carcinoma of the sigmoid enter the hospital with complete intestinal obstruction. In the proximal loop there is muscular hypertrophy, beginning to fail in power and dilatation, with stasis of intestinal contents. The net-result is a living test tube of bacteria of the highest virulence. Any anastomotic surgery directed against the septic upper loop carries with it a high incidence of mortality, from leakage or suture separation. Furthermore, sutures passed through such a diseased bowel are very apt to leak, even if

the suture line remains sufficient to prevent gross separation of the bowel segments. Peritonitis is the inevitable result. Another source of peritonitis is the rupture into the peritoneal cavity of an abscess arising from the catgut employed in the closure of the abdominal parietes. Hence, the use of interrupted wire sutures referred to previously.

With the complete defunctionalization of the distal loop, as obtains in the Devine colostomy, the obstructive phenomena are of no importance, the muscular layers of the bowel walls lose their edema and reacquire their normal tonicity. Stasis is no longer possible, the distended bowel lumen returns to its normal caliber, or even shrinks somewhat from physiologic disuse. Sutures placed in a bowel loop, thus restored to normal, will hold and not leak. Again, the bacterial flora of such a defunctionalized and therapeutically treated bowel is reduced to minimal numbers and virulence—in short, a reasonably aseptic bowel tube is obtained. When a neoplasm begins its lethal march in the bowel it early initiates certain physiologic and bacteriologic changes within the lumen of the bowel. There is an increase of peristalsis, a larger excretion of mucus and an increasing permeability of the bowel wall not infrequently leading to perforation. There then ensues a circumferential inflammation. In the area of the neoplasm there is increased vascularity, edema and infiltration with inflammatory cells. In fact, every neoplasm induces peripheral inflammatory changes, with fixation, loss of flexibility, and mobility of the bowel. Surgeons have been impressed repeatedly with the amount and degree of inflammation in the area of a bowel neoplasm, with fixation of the affected bowel to bladder, to the pelvic viscera in the female, to small intestines and omentum. Such secondary changes in the area of a neoplasm greatly increase the technical difficulties of resection, lessen the operability and largely increase the mortality and morbidity. When the distal loop is defunctionalized by a Devine colostomy these inflammatory changes resolve, largely disappear, local resistance is enhanced, fixation lessened, and mobility increased. The surgical gain is largely in increased operability, less mortality, fewer complications and more rapid recovery.

The theory and conception, as well as the practical application of the Devine colostomy is based upon defunctionalization of the bowel, with reduction of the sepsis and inflammation in the affected bowel. Upon these concepts, it is possible to extend the indications and usefulness of the Devine colostomy. It may be performed some days or weeks before resection or, occasionally, may be performed at the same time as the resection, although I do not recommend it as a simultaneous operation with resection except under very special circumstances. The Devine colostomy can be employed with great value in the following conditions:

SCOPE OF EMPLOYMENT OF THE DEVINE COLOSTOMY

ILLUSTRATIVE CASE REPORTS

I As a preliminary operation to an abdomino-perineal resection for carcinoma of the rectum. Not infrequently, carcinoma of the rectum is associated

with an extreme degree of inflammation. It is the latter and not the cancer *per se* that fixes the tumor to the bladder or pelvic viscera. With a Devine colostomy and local intraluminal therapy it is possible to bring about a great degree of resolution in the inflammatory process, and convert an inoperable carcinoma into an operable one.

Case 1—Male, age 69, complained of "loose bowels and lots of gas." A mass could be felt in the lower left quadrant and, on rectal examination, at 15 cm from the anal margin a flat, ulcerating growth, with almost complete obstruction of the upper rectum could be seen through the proctoscope. Biopsy revealed adenocarcinoma. The tumor mass was "frozen" in the pelvis, and a strong suspicion was entertained of metastases in the liver. By reason of the perirectal involvements, a palliative colostomy seemed to be the only procedure indicated. A Devine colostomy was performed, daily bowel function was readily obtained through the colostomy, and treatment of the distal loop instituted. Twenty-one days later a typical abdomino-perineal resection was performed. The technical procedures were carried out without undue difficulty. A terminal, left lower quadrant permanent colostomy was performed as a routine part of the abdomino-perineal resection with the plan of later reestablishing colon continuity by discontinuing the Devine colostomy. Without the preliminary Devine colostomy it would, in my opinion, have been impossible to accomplish an abdomino-perineal resection without a mortality.

2 As a preliminary operation for rectosigmoidal adenocarcinoma and by this means to permit a low end-to-end anastomosis and avoid an abdomino-perineal resection.

Case 2—Female, age 65, consulted her physician for "bleeding from the rectum." Under spinal anesthesia, a sigmoidoscope was introduced into the rectum and, 20 cm from the anal margin, an obstruction was encountered, with bleeding. Two biopsy-punch specimens were obtained which showed adenocarcinoma. A Devine colostomy was performed and intraluminal therapy was initiated through the distal colon. Twenty-seven days later, through a left lower rectus incision, the lower half of the sigmoid and rectum were mobilized down to the cul-de-sac, and a resection, with aseptic end-to-end anastomosis performed. The patient was discharged at the end of three weeks, returning to the hospital after an interval of three months. A Devine spur clamp was introduced, without any anesthetic, and the spur excised. The orifices of the Devine colostomy later closed spontaneously, aided by cauterization on three occasions. In this case an abdomino-perineal resection was avoided.

According to Miles, metastatic lymph node invasion of carcinoma of the rectum follows three separate and distinct paths. (1) The intramural system consists of two networks, one beneath the mucous membrane, and the other between the muscle layers, (2) the intermediary system consists of a subserous network, where the rectum is covered by peritoneum, and a lymph sinus where the rectum is not covered by peritoneum, and (3) the extramural lymphatic system of the rectum has (a) an upward zone of spread draining into the lymph nodes that eventually terminate in the angle of divarication of the iliacs from aorta and (b) the lateral zone of spread, which extends laterally involving the lymphatics of the levator ani, the prostate in males, the cervix and broad ligament in females, and (c) the downward zone of spread which extends toward the external sphincter, and the lower fibers of the levator ani. Rarely does a rectal cancer metastasize downward or into the groin.

The approach to the tumor in this patient through the abdomen, from above downwards, following the technic of an abdomino-perineal operation, permitted the surgeon to derive all the surgical benefits of the radical abdomino-perineal resection, and yet preserve the normal anus

3 As a preliminary (rarely simultaneously) operation for resection of a sigmoidal neoplasm

Case 3—Female, age 58, complained of pain in the lower abdomen moving transversely to the left and, for the same period, had noticed blood in the stool. Barium enema examination showed a definite, and somewhat irregular narrowing of the lumen of the colon at the junction of the sigmoid and descending colon for a distance of about seven centimeters. Operation revealed an annular carcinoma arising from the middle of the sigmoid, involving the entire circumference of the bowel, leaving a lumen approximately the size of a lead pencil. A resection, with a lateral sigmoidorectostomy was performed, and immediately followed by a Devine colostomy.

The patient made an uneventful recovery, except that 17 days after the resection—when we contemplated restoring colon continuity through the Devine colostomy loops—a barium enema showed some extravasation from the distal resected end of the sigmoid. With the functioning Devine colostomy, it was possible to take all the time that was necessary for the fistula to close. Intraluminal therapy in the distal loop could be continued, and the fistula was neither contaminated nor complicated by the seepage of stool. After four weeks at home the patient returned to the hospital, when a barium enema showed that the leakage had ceased. An Ochsner-DeBakey (Devine) colostomy clamp was applied. The spui was eciased within four days, and bowel movements *per anus* reestablished. The orifices of the Devine colostomy were cauterized on three different occasions, in the office, and closure allowed to proceed without any further care.

4 As a preliminary and temporary operation for acute perforating diverticulitis or "diverticular tumor" of the sigmoid

Case 4—Male, age 62, entered an hospital elsewhere, with a complete intestinal obstruction, due to a rectal mass, diagnosed as inoperable carcinoma of the rectum. A colostomy was recommended, together with roentgenotherapy. The patient entered the Post-Graduate Hospital. The obstruction was so complete that a barium enema could not be introduced. The patient's history was characterized by three significant features: (1) Intermittent pain in the left lower quadrant, (2) bladder irritability, with painful micturition, and (3) an absence of blood in the stools. On examination, the patient was found to have a mass in the left lower quadrant. On rectal examination, there was complete obstruction from a large, tender, pelvic mass. There was no rectal bleeding upon examination. A preoperative diagnosis of perforating diverticulitis of the sigmoid was made.

The operation consisted of a Devine colostomy through the right upper rectus muscle. On opening the abdomen a complete abdominal exploration was carried out with the following findings: The descending colon passed down, unimpeded into the sigmoid, where an infiltrating process involved the entire wall of the bowel and extended from the sigmoid to the junction of the rectum proper. There was a marked inflammatory reaction surrounding the mass, so that it was fixed to the lateral and posterior wall of the true pelvis. The small intestines seemed to be normal. The liver was without any palpable or visible evidence of metastases.

The patient left the hospital 15 days postoperative. Two months later, a barium enema, from below upwards to the left upper colostomy opening, did not show any roentgenographic evidence of obstruction. The beginning of the sigmoid for a distance of eight centimeters, showed irregularity and small pocket like diverticula. Roentgenologic examination from above downwards, through the left upper colostomy opening

did not show the presence of any obstruction Three and one-half months from the time of the Devine colostomy, an Ochsner-DeBakey spur clamp was applied, and bowel continuity reestablished One month later, the right colostomy wound closed spontaneously, and a few weeks later the left colostomy opening was closed, after two cauterizations of the mucous membrane and granulation tissue

5 As a preliminary and permanent colostomy for resection of the left colon and rectum for ulcerative colitis

Case 5—Female, married, aged 40, complained of diarrhea, and blood and mucus of two years duration, numerous bowel movements were accompanied by severe lower abdominal cramps Barium enema revealed no evidence of organic obstruction The proximal colon appeared somewhat atonic and distended, and there was luminal constriction with spasm in the distal colon and sigmoid The descending colon and sigmoid appeared rigid and tubular, due to chronic inflammatory changes During the course of the following year the patient developed multiple ischiorectal abscesses, with fistulae, and a destruction of the sphincter from continuous suppuration

Dr Z Bercovitz, of the New York Post-Graduate Hospital staff, was of the opinion that the rectal condition was part of a nonspecific ulcerative colitis and not lymphogranuloma venereum An exploratory celiotomy was performed through a right upper rectus incision, and revealed a chronic inflammatory change of the rectosigmoid, descending colon and rectum At approximately the midpoint of the transverse colon, the large bowel appeared to be normal A Devine colostomy was performed

Four specimens were taken from the rectum, about four inches above the anal margin, which showed acute and subacute inflammation, compatible with nonspecific ulcerative colitis The patient was discharged, with a functioning Devine colostomy on the 26th day after operation, to continue irrigations of the left bowel and intraluminal therapy at home For 13 months following the Devine colostomy the patient's general condition improved, the anemia disappeared, and there was a continuous gain in weight and well-being However, the rectal and bowel condition, although markedly improved, was not satisfactory Blood and pus were discharged intermittently from the rectum and the fistula A very distressing rheumatoid condition intervened, involving fingers, wrist, shoulders and knees After consultation with Dr Z Bercovitz, we came to the conclusion that nothing more was to be gained by continuing the treatment A complete resection of the left transverse colon, descending colon and sigmoid, combined with an abdomino-perineal resection, was carried out as a one-stage operation, through a left pararectus incision

The pathologic report was chronic ulcerative colitis, with stricture The patient made a rapid recovery, and was discharged on the 30th day postoperative The patient now has a right upper rectus, terminal colostomy, with good function Incidentally, the rheumatism began to improve immediately, and later disappeared

The plan of utilizing the technic of the Devine colostomy in this case was based upon the patient still having an apparently normal right colon Without the Devine colostomy I do not believe the same result could have been accomplished

6 As a temporary colostomy to correct a fistula following anastomotic surgery on the left colon

Case 6—Female, age 35, complained of intermittent abdominal pain of one year's duration Roentgenologic examination revealed an annular type of infiltrative lesion along the distal portion of the descending colon A resection, with a lateral colosigmoidostomy and cecostomy, was performed, in another clinic, for adenocarcinoma of the descending colon Seven days after the resection, stool began to appear through the abdominal wound The cecostomy was not functioning A catheter cecostomy has always seemed to me to be a very unsatisfactory operation It does not "detour" the

stool, and in about one-half the cases in which it is employed it fails to work after a few days or at least functions imperfectly. A Devine colostomy was performed on the 14th day after the primary resection. Obviously, from the time of the Devine colostomy there was no further discharge of stool from the left lower abdominal wound. The patient was discharged from the hospital on the 45th day postoperative, with a fully functioning Devine colostomy and a healed cecostomy and resection wound. After two months at home, a barium enema revealed a fully functioning side-to-side anastomosis in the lower part of the descending colon and colostomy openings of the mid-transverse colon. The patient reentered the hospital, and Devine spur clamps were applied, and fecal current through the left bowel reestablished. Later the orifices of the Devine colostomy closed gradually, without any surgical procedures. Barium enema 14 months later revealed a side-to-side anastomosis of descending colon, with an adequate patent stoma.

7 As a preliminary measure for cases complicated by intestinal, vesical or rectal fistulae

Case 7—Male, 30, entered an hospital elsewhere, complaining of bladder trouble. The clinical record notes "that upon cystoscopic examination there was on the posterior wall and dome of the bladder, a large infiltrating tumor." A biopsy specimen was obtained but reported "unsatisfactory for diagnosis." A celiotomy, through a midline suprapubic incision, revealed "pelvic colon intimately adherent to posterior wall of the bladder, incorporated with several loops of ileum. The entire mass was fixed to pelvis. No biopsy was taken. Colostomy was performed, with the descending colon through a left iliac stab wound." *Gross Diagnosis* "Carcinoma of the rectum."

Four months later, the patient entered the New York Post-Graduate Hospital, presenting a left lower quadrant loop-colostomy, great emaciation, anemia, a large pelvic mass of extrarectal origin, and an infected bladder, with pus and red blood cells in the urine. He had been receiving three or four injections of morphine each day for pain. An exploratory celiotomy was indicated, as the previous diagnosis of carcinoma of the rectum could not be sustained in the absence of any direct symptoms or signs of rectal involvement. In view of the very unsatisfactory colostomy, and a known pelvic tumor, it was decided to establish a Devine colostomy, and explore the abdomen.

Operation—The abdomen was opened through a right upper rectus incision and all the viscera in the upper abdomen were found to be normal. A simple loop-colostomy had been performed. Wedged in the pelvis was a mass, shaped very much like a large Idaho potato, fixed to the bladder, rectosigmoid, rectum and small intestine. A Devine colostomy was established to defunctionalize completely the left colon and rectum. After the Devine colostomy we were greatly chagrined to find that very little stool came through the right Devine colostomy orifice, but that profuse liquid stool continued to pour forth from the sigmoidostomy. As no material could pass through the transverse colon after the Devine colostomy, it was apparent that there must be a fistulous communication *via* the tumor into the rectosigmoid below the sigmoidostomy. Nine days later, after three transfusions, a celiotomy was performed through a lower midline incision. On opening the abdomen, the cecum was found lodged in the pelvis, markedly hypervascularized, and covered with chronic granulation tissue. The mass was fused to the base of the bladder and to the upper portion of the rectum within the rectovesical pouch. The last 18 inches of terminal ileum were one firm, agglutinated mass, attached to the cecum, bladder, and to the sigmoid below the colostomy opening. The picture was that of a typical inflammatory condition, secondary to intestinal perforation or to a previous appendiceal abscess.

The pelvic tumor was dissected free, *en masse*, from the bladder, rectum and sigmoid, and delivered into the wound. It was found that the tumor consisted entirely of the products of a subacute inflammatory disease of the head of the cecum, appendix and terminal ileum. There was a fistulous communication between this small intestinal-

cecal mass and the rectum about midway between the sigmoidostomy wound and the anus. The terminal ileum and cecum were resected, and an end-on-side ileocolostomy performed, using Furniss' clamps. Four sheets of rubber tissue were placed in the rectovesical pouch, and in the center of these was placed one strip of iodoform gauze saturated with Cutler's solution. The effect of the four sheets of rubber tissue was to exclude, completely, the pelvis from the upper abdomen. Into the peritoneal cavity above the pelvic rim was inserted five grams of sodium sulfathiazole. The abdomen was closed with Malin stainless steel wire.

The patient had a stormy convalescence for the first ten days but later gained seven pounds, and left the hospital 24 days after the resection, with a dry sigmoidostomy, clean bladder, and a good functioning Devine colostomy.

Pathological Report Regional ileitis, with multiple strictures and multiple sinus formation, and chronic lymphadenitis of the mesenteric lymph nodes.

By utilizing the technic of a Devine colostomy the surgeon can disregard—for an indefinite period—the entire left colon, sigmoid and rectum. The fistulous opening into the rectum below the sigmoidostomy will be allowed to heal naturally and the surgeon can reserve for a later and safer time the closure of the sigmoidostomy. In Case 7, a series of serious errors in diagnosis and treatment plus grave bowel complications, were overcome by employing a Devine colostomy as the pivotal point for surgical removal of the tumor.

It should be stated that in the Devine colostomy certain technical details need emphasis. There is a rather marked tendency for the development of postoperative herniation at the side of the Devine colostomy. This may, in a measure be obviated by making the Devine colostomy directly through the fibers of the rectus muscle. It is to be recalled that the fibers of the rectus muscle divaricate from the navel upward and outward to their insertion at the costal arches. This leaves an isosceles triangle with the base at the xiphoid cartilage and the apex at the navel that is devoid of muscle fiber. By placing the second incisions of the Devine colostomy in the middle of the belly of the rectus muscle and somewhat lower than described, this tendency for herniation is largely obviated. It is equally important that the loops of the Devine colostomy after emerging from the abdomen are intubed only through subcutaneous tissue before their exit on the skin. It is also equally important that in the ecrasement of the spur the Devine colostomy clamp be inserted well down and I think it is also well to have the patient in somewhat of a Trendelenburg position in bed when the clamp is applied, the small intestines will therefore, fall away from the double-barreled tubes, and the clamp can be inserted more deeply. It is also to be emphasized that the cutting-through of the spur should be adequate. It has been our custom after the clamp is removed, to introduce the index finger of each hand through the respective right and left colostomy orifices and "iron-out" and divulse the new stoma. Furthermore it has not been found necessary in our limited number of cases, to do anything to close the orifices of the colostomy after it has been decided to reconstitute colon continuity except to cauterize the orifices. In from three to six weeks both the orifices will close. There is a tendency after the right orifice is closed

for it to break open and occasionally allow the escape of some gas. The patient is usually distressed to find this occurring and a word of assurance that it will terminate in a short time usually allays his apprehension.

CONCLUSIONS

1 The Devine colostomy is a fundamental contribution to large bowel surgery.

2 Attention is directed to the basic principles underlying this procedure namely complete "defunctionalization and debacterIALIZATION" of the distal colon.

3 In a series of cases in which it has been employed it is evident that the range of application or indications for its employment may be widely extended.

4 The Devine colostomy is technically without difficulty. It is safe and easily controlled with reasonable care and gives a continent anus.

5 It may be employed as a preliminary or first-stage safety operation or continued as a permanent colostomy.

REFERENCES

- ¹ Mayo Charles H. and Dixon Claude F. A New Type of Permanent Colostomy. *ANNALS OF SURGERY* 87, No. 5, 711 May 1928.
- ² Devine H. B. Safer Colon Surgery. *Lancet* 1, 627 March 21 1931.
- ³ *Idem* Operation on a Defunctioned Distal Colon. *Surgery* 3, No. 2 165 February 1938.
- ⁴ *Idem* Carcinoma of the Colon. *Brit Med Jour* 2, 1245-1249 December 28 1935.
- ⁵ *Idem* The Surgery of the Alimentary Tract. Williams and Wilkins Co. Baltimore 1940.
- ⁶ Jackson Reginald H. Technique and Demonstrable Advantages of the Devine Colostomy. *Tr South Surg Assn* Vol LI December 6 1938. J. B. Lippincott Co. Philadelphia 1939.
- ⁷ Ochsner, Alton DeBakey Michael and Rothschild Joseph. The "Defunctionalizing" Colostomy (Devine). *J A M A* 113, 568 August 12, 1939.

METABOLIC STUDIES IN PATIENTS WITH CANCER OF THE GASTRO-INTESTINAL TRACT

VII—THE INFLUENCE OF GASTRIC SURGERY UPON THE CHEMICAL COMPOSITION OF THE LIVER*

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IN A PREVIOUS STUDY,¹ the chemical composition of the livers of patients subjected to gastro-intestinal surgery was determined. The segments of liver removed for chemical analysis were obtained as soon as the peritoneal cavity was entered. In 13 patients submitted to gastric operations, additional hepatic tissue samples were obtained at the termination of the operative procedures. The chemical analyses of these postoperative specimens, when compared with the analyses of the biopsies taken at the start of each operation, offer an opportunity to study the effects of the trauma incident to gastric surgery. The effects would include the influence of the anesthesia upon the chemical constituents of the liver.

Intra-abdominal surgical trauma of this degree does alter the metabolism, as indicated by an outpouring of nitrogenous end-products of protein metabolism during the immediate postoperative course.² Evidence of liver dysfunction following surgery, determined by hippuric acid test, is noted^{3,4}

A more exact understanding of the alterations of the hepatic constituents, therefore, may permit the preoperative, concurrent, and postoperative applications of methods suitable to combat any deleterious changes in the liver.

CLINICAL MATERIAL AND METHODS—Of the 13 patients used in this study, eight had gastric cancer and five had non-neoplastic diseases of the stomach. The operative procedures were grouped into 11 subtotal gastrectomies, one total gastrectomy, and one gastro-enterostomy. In several patients an average of 250 grams of glucose was administered during the ten hours prior to operation. The effects of the glucose on the composition of the liver are described in a previous communication.¹ The patients were given morphine sulphate gr 1/6, scopolamine gr 1/150, and nembutal gr m, from one to two hours before being taken to the operating room. All patients were anesthetized with spinal anesthesia (pontocaine). The spinal anesthesia was occasionally supplemented by inhalation or intravenous anesthesia (sodium pentothal) during the course of the operation. The anesthesia used in each instance is recorded in Table I. In every case, as soon as the operation was begun, intravenous fluids were administered, usually consisting of normal saline solution, whole blood, or both. The operating room was air-conditioned and maintained at a temperature of 78° F, and 50 per cent humidity.

Technic of Biopsy—At the completion of the operative procedure, and before the peritoneum was sutured, the liver biopsy was obtained from the inferior border of the left lobe, usually to the right of the region from which

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the biopsy had been taken at the start of the operative procedure. Different portions of the liver have approximately the same chemical composition, according to Rourke and Stewart.⁵ The liver biopsy was treated and analyzed by methods described in a previous publication.¹

INFLUENCE ON THE CHEMICAL COMPOSITION OF THE LIVER

The essential data are presented in Table I. Analysis of the figures for each hepatic constituent reveals the following changes:

Water—In most instances there was an increase in the total water content of the liver during the operative procedure. A decrease in the water content was found in one patient and a questionable decrease in two others. The average increase in the total liver water during the operation was 1.1 per cent. This is an interesting observation, since it has been demonstrated that during an operative procedure there is a loss of fluid varying from 500 to 2,000 cc.⁶ The administration of an average of 1,200 cc. of fluid to patients during the course of the operation on the stomach is probably compensated for by the loss consequent to abdominal surgery. The fact that the operating rooms were air-conditioned may be one possible factor contributing toward the loss of a minimum quantity of fluid during the operation.

Chloride-Space—An accurate estimate of the chloride-space before and after operation is not feasible (the term "chloride-space" is used in this paper to apply to that portion of the liver which is extracellular, and which may be used to represent the extracellular water).¹ The calculation of the chloride-space depends on the estimation of the plasma chloride.⁷ During the operative procedures, however, the patients received normal saline solution intravenously, with a continuation during the immediate postoperative course. This factor prevents an accurate estimation of the serum chloride, which is necessary for calculating the chloride-space of the organ.

However, a rough estimate of these values is possible. In five patients there was an increase in the chloride-space, but in seven there was a definite decrease. In several instances, the decreased chloride-space was associated with an increase of the total water in the liver. This indicates an increase in the water within the cell during the operation, in some instances at the expense of water in the extracellular position. Such figures demonstrate the marked variations in fluid exchange of the different patients subjected to surgery. It demonstrates that changes in hydration occur within the tissues during the operation and that a shift of the tissue water between the intra- and extracellular compartments takes place.

In some of the patients studied, there was an increase in liver lipid and decrease in glycogen during the operative procedures. Inasmuch, as glycogen is deposited with water, its loss from the liver would be associated with a loss of intracellular water.⁸ Furthermore, lipid is deposited in the liver without water, and an increase in hepatic lipid would tend to dehydrate the liver cell.⁸ Thus, during an operation, in which there is a loss of glycogen and gain in lipid, one would expect a decrease in hepatic water. The observation that an increase in hepatic cell water occurs during some surgical procedures indicates that exchanges of cellular water may occur.

independently of the hepatic glycogen, lipid and protein content

Glycogen—The liver loses glycogen during operations on the stomach. Pre- and postoperative glycogen values were obtained in ten patients. An average loss of 2.04 Gm per cent of glycogen occurred, with a range varying from 0.75 Gm per cent to 3.87 Gm per cent. The average preoperative hepatic glycogen value in the ten patients studied was 4.47 Gm per cent. Thus an average loss of 45 per cent of the glycogen content of the liver occurred during the operation. In those instances where the patient had a low preoperative glycogen level, the loss frequently exceeded 50 per cent and in one case (T. B.) the loss equalled 75 per cent of the total preoperative glycogen content. There was no constant, significant correlation between the level of the hepatic glycogen and the quantity lost.

The observation of MacIntyre, *et al.*,⁹ that no significant alterations of glycogen occur during operations, may possibly be explained in part by dehydration, and a corresponding concentration of glycogen, as they do not present values for the hepatic water. In the series presented here, the slight increase in total water may cause some dilution, but on plotting the intracellular water alteration against the alteration in glycogen, no correlation is noted. This indicates that the glycogen loss is real and not a result of alterations in hydration.

Lipid—There is a significant fluctuation of the hepatic lipid during the usual time consumed in these major gastric operations. Case J. R. cannot be considered as absolutely typical of this group, because in this patient the liver contained lesions of Boeck's sarcoid, and the pathologic involvement must have contributed somewhat to the chemical alterations. In the other 11 patients, in whom determinations were secured there was an increase of hepatic lipid in seven, and a decrease in four instances. There was evidently no relationship between the initial hepatic lipid level and the loss or gain in hepatic lipid during the operation. No relationship was observed between the anesthesia employed and the postoperative lipid content of the liver, nor did the duration of the operation significantly alter the postoperative hepatic lipid content. When a gain of lipid was observed, the fact may be interpreted as representing an influx of fat to the liver under the stress of the major operative procedure. In those instances where a decrease in the lipid content occurred, it may be the result of catabolism of the lipid for purposes of energy.

Protein—The total protein in the livers of four patients increased during the operations, in one patient there was no alteration, and the protein content of the livers of six patients decreased during the operative procedures. The average gain in protein of the four patients was 1.1 Gm per cent and the average loss in hepatic protein of the six patients was 1.1 Gm per cent. No definite interpretations can be derived from these changes, except that they do show the rapid rate of exchange that hepatic proteins undergo, and demonstrate that they are engaged in active metabolic changes and are not inert structural units.

Alterations in the "albumin" and "globulin" fractions of the liver proteins during the course of an operation yields the following information. In the

11 patients studied, an increase in the albumin fraction in the postoperative specimens occurred in eight instances, and a decrease occurred in two. In one case, no alteration was noted. The average change of all determinations was an increase of 0.88 Gm per cent of albumin. The increased albumin was usually associated with a decrease in globulin content. In two patients, there was an increased hepatic globulin (average 0.66 Gm per cent). In one patient there was no alteration, and in seven patients, the decrease in hepatic globulin averaged 1.48 Gm per cent. The over-all alteration of the hepatic globulin in the ten patients was a loss of 0.9 Gm per cent. These alterations might be interpreted as representing a change of the hepatic protein fractions during the period of operative stress. The physiologic implication of this alteration is not apparent.

CONCLUSIONS

(1) In 11 patients studied there was an average increase of one per cent hepatic water during the course of a subtotal gastrectomy. The intravenous administration of fluids during the operative procedures apparently compensates for any fluid lost during the operation.

(2) A shift of fluid between the intra- and extracellular positions within the livers occurred during operative procedures on the stomach.

(3) An average loss of 45 per cent of the hepatic glycogen occurred during the operation.

(4) Total hepatic lipids increased during surgical intervention. The average increase was 1.97 Gm per cent.

(5) There was a fluctuation in the content of hepatic protein, with an increase in hepatic albumin and a decrease in hepatic globulin during the operation. The physiologic implication of the protein alteration is not apparent.

REFERENCES

- ¹ Ariel, I., Pack, G. T., and Rhoads, C. P. Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract. VI. The Chemical Composition (Protein, Glycogen, Lipid, Water) of Liver in Patients with Gastro-intestinal Cancer. (In press)
- ² Ariel, I., Pack, G. T., and Rhoads, C. P. Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract. VI. Nitrogen Balance Studies in Patients undergoing Abdominal Surgery, and the Incidence of Postoperative Hypoproteinemias in Patients with Gastric Cancer. (In press)
- ³ Boyce, F. F., and McFetridge, E. M. Studies of Hepatic Function of the Quick Hippuric Acid Test. III. Various Surgical States. *Arch Surg*, **37**, 443-455, 1938
- ⁴ Schmidt, C. R., Unruh, R. T., and Chesky, V. E. Clinical Studies of Liver Function. I. The Effect of Anesthesia and certain Surgical Procedures. *Amer Jour Surg*, **57**, 43-50, 1942
- ⁵ Rourke, B. A., and Stewart, J. D. Composition of the Liver. Its Uniformity with respect to the Concentration of certain Biochemical Constituents in Different Parts of the same Liver. *Arch Path*, **33**, 603-606, 1942
- ⁶ Collen, F. A., and Maddock, W. Dehydration Attendant on Surgical Operations. *J A M A*, **99**, 875-880, 1932
- ⁷ Hastings, A. B. The Electrolytes of Tissues and Body Fluids. The Harvey Lectures. *Series* **36**, 91-125, 1940-41
- ⁸ Fenn, W. O., and Haeghe, L. F. The Deposition of Glycogen with Water in the Livers of Cats. *Jour Biol Chem*, **136**, 87-101, 1940
- ⁹ MacIntyre, D. S., Pederson, S., and Maddock, W. G. The Glycogen Content of the Human Liver. *Surgery*, **10**, 716-729, 1941

BRIEF COMMUNICATIONS



CHOLECYSTECTOMY WITHOUT DRAINAGE

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DRAINAGE OF THE LIVER BED is still employed as a routine procedure by most surgeons in the operation of cholecystectomy

Many years ago we were discussing the subject of drainage with Dr Harry Richter, and were impressed with the results he had obtained in a series of cases in which the abdomen was closed without drainage. Furthermore, we were mindful of the fact that any drainage material—a soft or hard rubber tube, a piece of penrose tubing, a strip of gauze, etc,—might act as a foreign body, and thus interfere with the healing of the liver bed or the stump of the cystic duct and, therefore, from a theoretical point of view, at least, be a menace rather than a factor of safety. Also, about that time we were called in consultation to see a patient who had developed a bile peritonitis following cholecystectomy, where the surgeon, following the usual custom, had “drained”, and yet, at operation, we found many quarts of bile in the peritoneal cavity. All these facts made us decide to attempt closure without drainage.

We, therefore, gradually abandoned drainage in carefully selected cases. Our operative technic remained the same—in brief, as follows: Right paramedian or transverse incision, careful exploration of abdominal cavity, exposure of gallbladder, exposure of cystic duct, careful inspection and external examination of common duct in all cases, and choledochotomy, with internal examination of the duct when indicated (about 15 per cent of cases)*, ligation of cystic duct with single catgut ligature, division of cystic duct, clamping, cutting and ligating cystic artery with single catgut ligature, removal of gallbladder from bottom up, suturing peritoneal flaps over gallbladder bed, only if this step is necessary to control oozing, and conventional closure of abdominal incision.

As we had the opportunity of seeing more and more patients operated upon without any ill results from the omission of drainage we became more and more convinced of the advantages of not draining. We feel that the postoperative course is cleaner and smoother, and the morbidity less. As a direct result of these observations, we have adopted, more or less, the following procedure. In uncomplicated cholecystectomy for chronic cholecystitis,

* Our indications are (1) Patient jaundiced at time of operation, or if attacks of jaundice, (2) common duct dilated, and (3) palpation of stones in common duct. Most cases of choledochotomy were drained.

with or without cholelithiasis—it is rare that we operate for cholecystitis without cholelithiasis—we omit drainage. If complications such as abscess formation, extremely dense adhesions which might contain residual infection, or oozing from the liver bed, are present then we either drain or not, depending upon the individual aspects of the case. In acute cholecystitis, or whenever the common duct has been opened we usually drain, although, here, too, we weigh the individual merits, and have, on occasions, omitted drainage, with very satisfactory results.

In order to inform ourselves of the correctness of our position, we have recently reviewed the last 500 gallbladder tract operations performed by one of us (R. B. B.). We found that 373 simple cholecystectomies were performed in nonacute cases in which the common duct was not opened.

In this series of 373 consecutive cholecystectomies, the abdomen was closed without drainage in 306 instances, and some type of drainage was employed in 67 cases. The mortality for the entire group of 373 cases was five or 1.3 per cent. The cause of death was postoperative pneumonia in one case, in two, the result of evisceration, in one, pulmonary embolism on the ninth day, and in one, the cause was unknown (a female, age 70, with a marked hypertension, who died with symptoms which led us to diagnose coronary occlusion). No postmortem was obtained in this case. These deaths all occurred in the nondrained cases, but none of these could be attributed to the omission of drainage.

Serious postoperative complications occurred six times in the 306 undrained cases, namely, four eviscerations and two postoperative pneumonias, one of the pneumonias eviscerated, and later developed a subphrenic abscess. None of these patients died. (These cases of evisceration, as well as those two quoted in the mortality list, all occurred in one or the other of those groups of eviscerations which we noted [Bettman and Lichtenstein. *Arch. of Surg.*, 32, 721, 1936] when we reviewed all the cases of evisceration which had occurred over a ten-year period, at Michael Reese Hospital. At that time, we could not explain either the cause of evisceration or the peculiar grouping of the cases, and, although much research work has since been devoted to the problem, we are still uncertain that any of the theories thus far advanced will explain all cases.)

Serious nonfatal complications developed six times in the drained cases, or 8.9 per cent—one instance of hemorrhage, three cases of subphrenic abscess, one pneumonia, with pleural effusion, and one of massive collapse of a lung. All of these patients, likewise, recovered. That a proportionately higher ratio of postoperative complications should develop in the drained cases, as compared to the undrained (8.9 to 1.3 per cent), is easily understandable because drainage was resorted to in those operations in which pathologic conditions seen at operations made us decide to depart from our usual procedure of not draining.

In no case in this series did a so-called "bile peritonitis" develop. During

this time we have seen in consultation three cases of bile peritonitis following simple cholecystectomy. In every case they had been drained. In two cases, little bile-colored fluid had escaped along the drain, and yet, at the second operation, the peritoneal cavity contained several quarts of bile. In one case the bile drainage had been profuse, but, in spite of this, a large amount of bile had found its way into the general peritoneal cavity and had produced the symptoms.

We were interested in the recent report of eight cases of bile peritonitis by Charles W. McLaughlin, Jr. (*ANNALS OF SURGERY*, 113, No. 6, June, 1941) before the Central Surgical Association, in which in the discussion he said "In this series all of these cases, with one exception, were drained."

What happens to the bile-stained drainage, which is almost invariably seen in those cases in which a drainage tube is used? This is a question which we are frequently asked. We cannot answer this, other than to say that we think it does not occur in the absence of a drainage tube. We say this because of the smooth and uncomplicated convalescent period associated with our nondrained cases, and, also, because there was no bile-staining of the peritoneal fluid seen in the four cases that came to autopsy, or in the five cases of evisceration.

SUMMARY—We are reporting a series of 373 consecutive cholecystectomies without choledochotomy performed by one of us, (R. B. B.), in which no drainage of the peritoneal cavity was employed in 306 cases, and some form of drain was introduced in 67 cases. There were five deaths in the entire series, or 1.3 per cent, but in none of these did the fact that no drainage was used play a rôle. Among the undrained cases, six, or 1.9 per cent, had serious, but nonfatal, postoperative complications, but, again, none of these could be attributed to the omission of drainage. There were six cases, or 8.9 per cent, among the drained cases who had serious postoperative complications, but here, also, none could be attributed to the presence of the drain. The proportionately higher percentage of complications in the drained group is readily explained on the basis of the pathology which caused us to drain.

CONCLUSIONS

We feel that, as a rule, it is perfectly safe, and, on theoretical grounds probably desirable, to close the abdomen without drainage following simple cholecystectomy, in which choledochotomy has not been performed.

This discussion does not include cases of acute cholecystitis, in which the omission of drainage may or may not be desirable.

We have been pleased with the clean and easy convalescence in this group of patients.

In short, we, ourselves, do not drain the peritoneal cavity following cholecystectomy unless specially indicated.

SPONTANEOUS EXTERNAL BILIARY FISTULA

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AND

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UPPER DARRY, PA

THE OCCURRENCE of spontaneous internal biliary fistula is very uncommon and according to Borman and Rigle¹ only 60 cases had appeared in the roentgenologic literature up to 1937. They further stated that gallstones have been vomited from the stomach, coughed up from the bronchial tree,

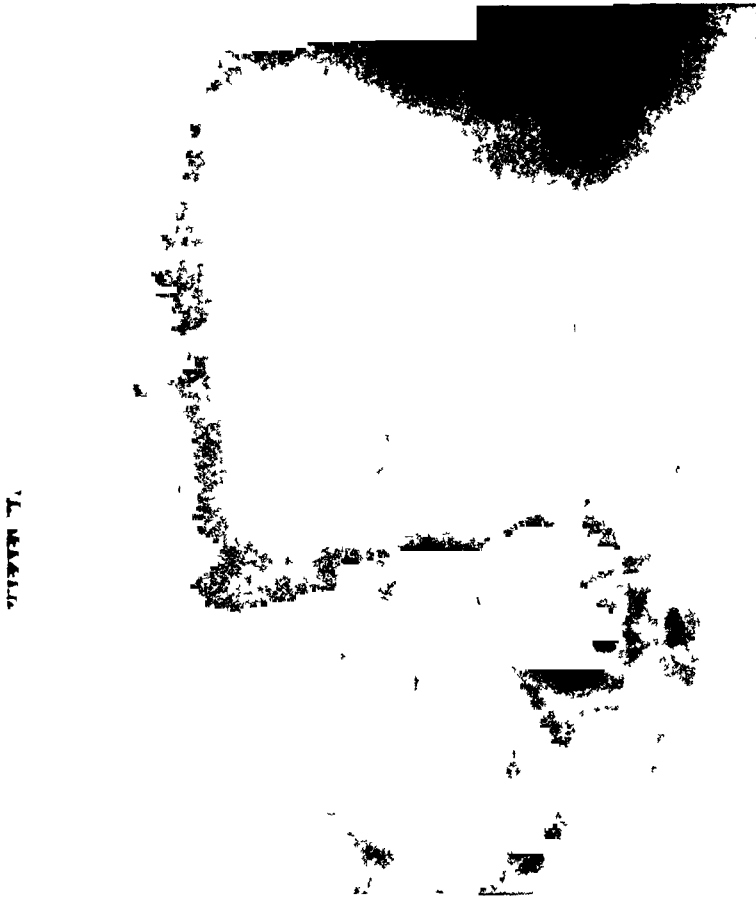


FIG 1—Lipiodol injection of sinus tract

voided in the urine, and frequently passed by the rectum, but no mention was made of stones being passed externally through the abdominal wall. The extreme rarity of spontaneous external biliary fistula prompted the report of the following case.

Case Report—N. B., male, age 78, first appeared in the Surgical Dispensary of the Delaware County Hospital, August 20, 1940, and gave the following history: Ten years previously he had a typical gallstone colic, with severe pain, which recurred at irregular intervals for the following year, lasting two to three days each time. The next attack was in 1938, and was no different from the former attacks. In February, 1940, a painless lump appeared just below the right costal margin, one inch lateral to

the mammary line, which gradually increased in size, became more superficial and, August 8, 1940, ruptured spontaneously through the overlying skin. The discharge contained pus and several small gallstones but no bile.

Examination August 30, 1940, revealed him to be well preserved for his age, weighing 150 lbs. When the dressing, that he had applied, was removed it was moderately stained with mucopurulent discharge and six small gallstones were found lying on the skin about the fistulous opening, which was six millimeters in diameter. There was no evidence of acute inflammation. After clearing the fistula of several additional stones with a small spoon probe, lipiodol was injected into the fistulous tract. A roentgenogram taken immediately was reported by Dr. P. A. Bishop, roentgenologist, as follows: "The lipiodol collects in a cavity that has a size, shape and position consistent with a gallbladder. It is not completely filled and there are irregular filling defects in the upper end of the gallbladder due to nonopaque calculi. The cystic and common duct are filled with the radiopaque oil and a small amount passed into the duodenum" (Fig. 1). Two days later an oral cholecystogram was reported as follows: "The gallbladder is not visualized. Opinion: Nonfunctioning gallbladder."

He was followed at regular intervals in the clinic until May, 1941, during which time the fistulous tract remained open, occasionally discharged a stone but no bile. There never was any evidence of acute inflammation, patient was never jaundiced and the stools were always of good color. Since this date we have been unable to contact the patient. Surgery was deferred because of his advanced age and the absence of obstructive symptoms.

SUMMARY

- 1 Spontaneous external biliary fistula is extremely rare and warrants the report of cases.
- 2 An instance of spontaneous external biliary fistula is hereby reported.

REFERENCE

- ¹ Borman, C. N., and Rigler, L. G. Spontaneous Internal Biliary Fistula and Gallstone Obstruction. *Surgery*, 1, 349-378, March, 1937.

CALCIFIED UNILOCULAR CYST OF THE SPLEEN

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OF THE SPLENOMEGALIES those due to cysts and neoplasms constitute a curiously low percentage. Because the spleen acts somewhat as a blood filter it may at least be expected that secondary carcinoma would occur frequently.¹ Such, however, is not the case. In a series of 40,000 surgical cases in the Boston City Hospital, reported² in 1940, there were only two instances of splenic neoplasms. That there is some special oncolytic substance present in the spleen is an idea not supported by conclusive evidence.³ Certainly, secondary tumors of the spleen are as frequent as those of the kidney.² In fact, 17,400 autopsies (Philadelphia General Hospital, reported³ in 1927) revealed 93 neoplasms of the spleen, the greatest number of which were metastatic carcinomas from the breast. Even thus, it appears that the spleen is particularly antagonistic to tumor cells—an observation which has been variously explained on anatomic bases, such as the limited number of subcapsular lymphatics or the sharp angle of the splenic artery, and on physiologic bases such as hostile splenic ferments or the pulsations of the spleen tending to prevent tumor cell lodgments.

It has been suggested⁴ that the etiology of a neoplasm must be considered as a separate problem for each organ of the body. This suggestion is lent material weight by the fact that the spleen, although occupying an apparently vulnerable position, is so stubbornly resistant to tumor cell invasion and growth.

From the foregoing, it may be inferred that neoplastic cysts of the spleen occur so infrequently that they may be considered medical curiosities. Indeed, up to January, 1941, only 108 nonparasitic cysts of the spleen had been reported.⁵ Classification of these cysts on a pathogenetic basis, as proposed by Fowler,⁶ would, at first glance, appear to simplify the problem of pathologic diagnosis. But the cause, in many cases, cannot be determined from the terminal histologic picture of a cyst, and until further definite knowledge is available as to the exact etiologic factors concerned in the production of splenic cysts it may be advisable to cling to a morphologic classification as suggested by Sherwin, Brown and Liber.⁷ This classification, a non-committal one, is as follows:

- (1) Large solitary cyst with hemorrhagic contents. This may be one of Fowler's neoplastic, traumatic or degenerative cysts.
- (2) Large cyst with satellites. This may be neoplastic or infoliate in nature.

(3) Multiple small cysts—the usual type

(4) Polycystic spleen

Because we can find records of only one case of splenic cyst, diagnosed roentgenologically before operation,⁸ and another of a calcified unilocular cyst of the spleen,⁹ we are reporting this case of large solitary calcified cyst of the spleen, suspected before surgery, and removed successfully, concomitantly with an acutely inflamed appendix, which had colored the clinical picture to no small degree

Case Report—J F W, white, male, age 41, awoke at 3 00 A M, May 1, 1942, with a generalized abdominal pain associated with slight nausea. Gaining no relief through drinking hot coffee, walking around, or attempting to defecate, he reported to the dispensary, where palliative treatment was without result. The patient was then sent 120 miles by automobile to the hospital and admitted to the Medical Service.

Nothing in the patient's history was apropos to his present complaints. He had never had a similar attack, and had had no operations or injuries. His bowel movements had been regular, and his appetite, as well as his general health, had been excellent.

Physical Examination—The patient was moderately obese, well-developed, with no visible evidence whatever of disease. There was slight rigidity of the abdominal muscles, pain upon deep palpation at McBurney's point and a rebound tenderness from the left to the right lower quadrant. Tympanites were moderate. A rather marked succussion sound was noted in the left lower quadrant which prompted a more thorough examination of this region. Because of the rather thick panniculus adiposus and some muscle rigidity it was difficult to demonstrate definite abnormality in the left lower quadrant. However, percussion with digital examination was sufficient to locate a mass whose upper border if projected, would fall above the level of the crest of the ilium. Rectal examination was negative. Heart and lungs were normal. Blood pressure 125/85. Temperature 99° F. Pulse 82. Respirations 20. **Laboratory Data**—R B C 6,000,000 hemoglobin 90% W B C 16,900, with 90% polymorphonuclear leukocytes. Urinalysis negative, Kahn test negative.

Preoperative Course—May 1, 1942. A diagnosis was made of acute appendicitis and the patient was transferred to the Surgical Service. Because of the ill-defined left abdominal mass and the question of differential diagnosis, it was decided to postpone surgery until more definite data were available.

May 2, 1942. The patient was apparently worse than on the preceding day. Temperature ranged from 99.4° to 101.2° F. Tympanites became pronounced. A roentgenogram of the abdomen revealed a cystic mass 14 cm in diameter with a partially calcified wall, to the left of the spinal column, extending inferiorly from the body of the third lumbar vertebra to the sacrum, and laterally to within four centimeters of the crest of the left ilium.

May 3, 1942. The condition of the patient was much worse. Intra-abdominal cysts of the male were considered differentially, including those of the spleen, mesentery, kidney and pancreas, along with cystic tumors of the stomach, intestines and accessory sex organs. A diagnosis was made of pedunculated cystic tumor (possibly of the spleen) with torsion of its pedicle. And because the patient's condition allowed no further temporization, surgical intervention was decided upon.

Operation—Under spinal anesthesia the abdomen was opened through a midline incision, revealing a free, odorless fluid, rather viscid and brown in color. Plastic exudate covered some of the coils of the small intestine. The presenting surface of the tumor was of even contour, white, and the distant periphery was a dark blue. Further exploration showed the tumor to be pedunculated (without torsion), and that it was attached intimately to the lower pole of the spleen. There were also

many fine adhesions extending from the mass to all surrounding structures. In removing the tumor its pedicle was severed with but little bleeding, and the stump of the spleen was covered over with some of the loose tissue which surrounded the base of the pedicle. Examination of the region of the cecum disclosed an abscess lateral to the large bowel, and a gangrenous appendix, from the base of which fecaliths had been extruded and through which gas was escaping. Because of the immobility of the cecum and its extreme friability, the opening into it through the base of the appendix was not closed after the appendicectomy. Instead, a Penrose drain was inserted and led through an abdominal stab wound. Sulfathiazole powder was liberally dusted over the abdominal contents, and the operative incision was closed tightly, in layers.

Postoperative Course—Except for a dehiscence of the wound, which was repaired effectively in the fourth week postoperative, the convalescence was uneventful. The patient was discharged to full duty two months after his admission to the hospital.

Pathologic Examination—*Gross* The specimen is an ovoid cystic mass, measuring $13 \times 12 \times 9\frac{1}{4}$ cm, one pole of which presented the stump of a pedicle, measuring 6×3 cm. At least one-half of the surface of the cyst is covered with a layer of splenic-appearing tissue one centimeter thick. Incision into the thin portion of the wall reveals it to be about three millimeters in thickness, and is composed of three distinct layers, the middle one of which is much softer than the inner and outer layers. Portions of the cyst wall are definitely calcified and cannot be cut with a knife. The uncalcified areas of the wall are leathery. The cyst contents, approximately 500 cc, have the color and consistency of cream-of-tomato soup. Fat globules float on the surface. It is odorless. With reflected light through the walls of a test tube containing the material, innumerable white, refractile objects can be seen giving the fluid the appearance of crystalline sludge. The inner surface of the cyst appears much like an old arteriosclerotic aorta with its raised yellow patches and streaks, calcified plaques overlying soft pulaceous material, and ulcerations with ragged margins. An inner shelf nearly surrounds the cyst at its equator, producing the impression that there had previously been two cysts which had coalesced.

Microscopically, sections through the thin portion of the wall show the three distinct layers of tissue, previously mentioned. The inner and outer layers are composed of hyalinized connective tissue. The inner layer is lined by a definite, highly refractile limiting membrane. The middle layer consists of essentially normal splenic tissue, continuous with the thick portion of spleen covering the rest of the cyst. The malpighian corpuscles, with their eccentric arteries, are small but distinctly developed. The trabeculae are normal in quantity, however they are pressed obliquely, some nearly paralleling the inner lining of the cyst. The vessels have thickened walls, and there is an increase in the reticular connective tissue elements of the splenic pulp. Sinusoids are dilated and empty. Microscopic examination of the cyst fluid shows fat globules of varying sizes, degenerated red blood cells, and cholesterol crystals. Chemical analysis of this fluid reveals occult blood four plus, total fat 12.04 gm per cent, and cholesterol 3.45 gm per 100 cc.

COMMENT—Because a layer of apparently normal splenic tissue surrounds the cyst, it cannot be considered that this lesion is the result of an old infarct, inasmuch as the spleen has no capsular circulation to keep alive any superficial layer in infarcted areas.¹⁰ The calcification in the cyst wall, and the degenerative nature of the cyst contents, place the tumor in the category of an old process—probably an hematogenous one several years previously. That the cystic tumor represents a true neoplasm of the spleen cannot be proved by its terminal histologic appearance and present data regarding splenic tumors. No stretch of the imagination is required, however,

to think of it as the result of an intrasplenic hemangioma, increasing pressure from which finally cut off its vascular supply

In passing, it may be stated that once again has been emphasized the danger of explaining rather clear-cut clinical symptoms with an incidental physical finding. A diagnosis of acute appendicitis probably precludes any delay in action caused by attempts to ascertain the nature of a second lesion.

SUMMARY

Because of the rarity of splenic cysts, this report is made on a large unilocular calcified cyst, suspected before surgery, and successfully removed without disturbing the uninvolved portion of the spleen. Review of available literature¹¹ would place this as the 155th case report of nonparasitic cysts of the spleen.

REFERENCES

- ¹ Boyd, William. Textbook of Pathology. 2nd Ed., page 802, Lea and Febiger, W., Philadelphia, 1934.
- ² Goldberg, Samuel A. Primary Splenic Neoplasms. Amer Jour Clin Path, 10, No 10, 700, October, 1940.
- ³ Krumbhaar, E. B. The Incidence and Nature of Splenic Neoplasms. Ann Clin Med, 5, No 9, 833-860, March, 1927.
- ⁴ Cramer, William J. A. M. A., 119, No 4, 311-316, May, 1942.
- ⁵ Watts, Duval, and Warthen, Harry J. Nonparasitic Cysts of the Spleen. Southern Surgeon, 10, No 1, 34, January, 1940.
- ⁶ Fowler, R. H. ANNALS OF SURGERY, 74, 20, July, 1921.
- ⁷ Sherwin, Benjamin, Brown, Chester R., and Liber, Amour F. Cystic Disease of the Spleen. ANNALS OF SURGERY, 109, No 4, 615, April, 1939.
- ⁸ Benton, Roy W. Large Cysts of the Spleen. J. A. M. A., 99, 1674-1676, November, 12, 1932.
- ⁹ Scotson, F. Hector. Calcified Cyst of Spleen. Brit Med Jour, Part I, 367, March, 1933.
- ¹⁰ McCallum, W. G. A Textbook of Pathology. 7th Ed., page 34, W. B. Saunders,

ADDITIONAL REFERENCES FOUND IN THE LITERATURE

1940

- a Cole, Frank L., and Forsee, James H. Cavernous Hemangioma of the Spleen. Surgery, 8, No 4, 639, October, 1940.
- b Garlock, John H. Primary Angiosarcoma of the Spleen. Jour Mt Sinai Hospital, 6, No 6, 319, March-April, 1940.
- c Booney, Charles M. Primary Malignant Tumors of the Spleen with Report of a Case of Lymphosarcoma. Jour Lab and Clin Med, 25, No 4, 630, January, 1940.
- d Starr, Frederic N. G. (Canada), ANNALS OF SURGERY, 98, 919, November, 1933.
- e Montgomery, Albert H., McEnery, Eugene T., and Frank, Albert A. Epidermoid Cysts of Spleen. ANNALS OF SURGERY, 108, No 5, 877, November, 1938.
- f McLaughlin, Charles W., and Beck, James S. P. Multilocular Cystic Lymphangioma of the Spleen. Arch Path, 15, 655-664, May, 1933.
- g Shawan, Harold K. Epidermoid Cysts of the Spleen. Arch Surg, 27, 63-64, July, 1933.
- h Frank, L. Wallace. Solitary Cysts of the Spleen. Southern Med Jour, 23, No 3, 212, March, 1930.

- i Andrews, F T, and Morter, R S Solitary Cyst of the Spleen Jour Michigan State Med Soc, 38, No 3, 201-204, March, 1939
- j Tomlinson, Wray E Primary Multiple Microcystic Lymphangioma of Spleen West Virginia Med Journ, 37, 24-25, January, 1941
- k Case Records of the Massachusetts General Hospital 222, No 25, June 20, 1940
- l Roberson, Foy Solitary Cysts of the Spleen ANNALS OF SURGERY, 3, No 5, 848, May, 1940
- m Nesler, A B, Faber, Luke, and Leik, D W Hemangioma of the Spleen with Spontaneous Rupture Jour Iowa Med Soc, 29, No 11, 566-568, 1939
- n Haines, Charles Everett, and McIlroy, P T Spontaneous Rupture of Cavernous Angioma of Spleen J A M A, 100, 1862-1863, June 10, 1933
- o Langenstrass, Karl H, and Newmann, Meta Reticulo-Endothelial Sarcoma of Spleen Arch Path, 20, 752-759, November, 1935
- p Caldwell, George T Endothelioma of the Spleen Report of Case Southern Med Jour 26, No 2 120-124, February, 1933
- q Grove, Lon W Fibro-Angioma of the Spleen ANNALS OF SURGERY, 105, No 6, June, 1937
- r Biller, S B Primary Endothelioma of the Spleen Arch Path, 25, 534-538, April, 1938
- s Alessandri, Roberto (Rome, Italy) Experience with Surgery of the Spleen Jour Mt Sinai Hospital, 4, 489-500, March-April, 1938
- t Schottenfeld, Lewis E, and Wolfson, William L Cavernous Hemangioma of the Spleen Arch Surg, 25, 867-877, November, 1937
- u McClure, Roy D, and Altemeier, W A Cysts of the Spleen ANNALS OF SURGERY, 116, No 1, 98-102, July, 1942
- v Deneen, Edward U Hemorrhagic Cyst of the Spleen ANNALS OF SURGERY, 116, No 1, 103-108, July, 1942

TRAUMATIC DIAPHRAGMATIC HERNIA WITH COMPLETE TEARING OF THE MEDIASTINAL PLEURA

REPORT OF A CASE

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THE SUBJECT of diaphragmatic hernia, including discussions of symptoms, diagnosis, and operative approaches, has been adequately described in the literature by Harrington, Schiffbauer, Truesdale and others. The case herewith reported is of particular interest because of the extensive injury to the diaphragm and also because the anterior mediastinal pleura was completely torn, so that the two hemithoraces communicated.

Case Report—The patient was a very strong and well-developed man, age 31. He was in an automobile accident in which two cars collided head on, traveling at a high rate of speed. He was unconscious following the accident until the next day, remaining in a hospital near the place where the accident occurred for three weeks, and was then moved to Denver. When first seen he was complaining of some difficulty in breathing and occasional cramping abdominal pains, suggestive of intestinal obstruction. He also complained of pain in the left shoulder.

On examination, there was dullness and absent breath sounds over the left chest as high as the fourth intercostal space posteriorly. There were also gurgling sounds to be heard over this area, which were suggestive of gas moving through the intestine. Roentgenologic examination following a barium meal showed the stomach and colon to be in the chest, extending as high as the third rib anteriorly (Fig 1).

A diagnosis of traumatic hernia of the left side of the diaphragm was made, and surgical intervention decided upon. On the day preceding the operation for repair of the diaphragm, the left phrenic nerve was crushed through an incision above the clavicle. The operation for repair of the hernia was undertaken under intratracheal anesthesia with cyclopropane.

Operation—The incision followed the seventh left intercostal space from the angle of the ribs to the costochondral junctions. The seventh and eighth ribs were divided at their angles to facilitate the exposure. On opening the pleura, the stomach, small intestine, colon, omentum and left lobe of the liver were found in the chest. There was no hernial sac. However, the most startling finding was a complete tear of the anterior mediastinal pleura, so that both sides of the chest were wide open and both lungs collapsed. Also, the pericardium was completely torn away from its diaphragmatic attachment (Fig 2). Surprisingly enough, the anesthetist had no difficulty in controlling the patient's breathing, even though there was complete bilateral pneumothorax. He did not find it necessary to use a great deal of positive pressure. The tear in the diaphragm was found to extend from a point about two inches to the left of the xiphoid process through the esophageal hiatus (Fig 3). After replacing the abdominal viscera the esophageal hiatus was reconstructed and the diaphragm repaired with interrupted No. 5 silk mattress sutures. Additional No. 2 silk interrupted sutures were used along the edges of the torn diaphragm. No attempt was made to repair the mediastinal pleura. The incision in the chest wall was closed with pericostal sutures of No. 2 catgut and interrupted silk sutures. Before placing the last sutures, a catheter was introduced into the pleural cavity in order to withdraw the remaining air after inflating the lungs. No drainage was instituted. An indirect transfusion of 500 cc of citrated blood was administered, and the



Fig. 1.—Preoperative roentgenogram of the chest taken after barium meal. The stomach and colon occupy a position high in the left thorax.

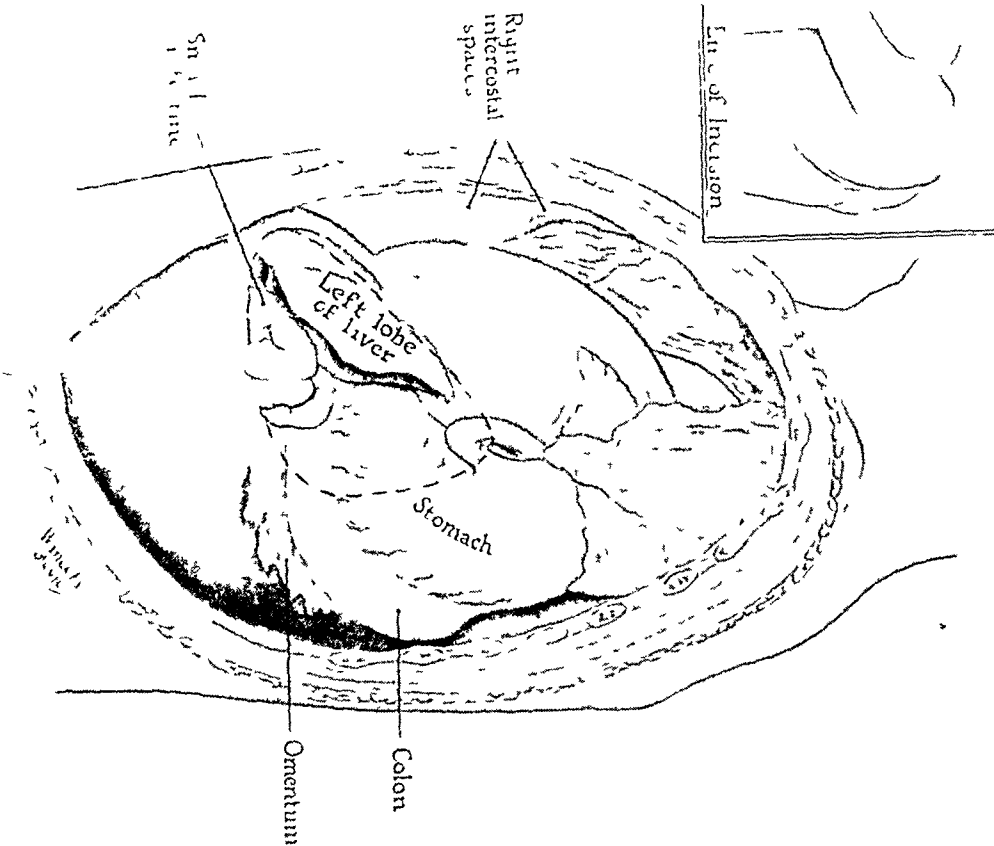


Fig. 2.—Drawing showing the relative position of the organs as they appeared when the chest was opened.

patient placed in an oxygen tent. A stomach tube which had been introduced before the operation was started, was connected to a Wangenstein suction apparatus.

The patient's postoperative course was essentially uneventful. At no time was it necessary to remove fluid from the chest. The patient has returned to work. Subsequent examinations, and roentgenograms taken at intervals of three months (Fig 4) and one year following the operation show no recurrence of the hernia.

DISCUSSION—A case of extensive traumatic rupture of the diaphragm and mediastinal pleura following an automobile accident has been described.

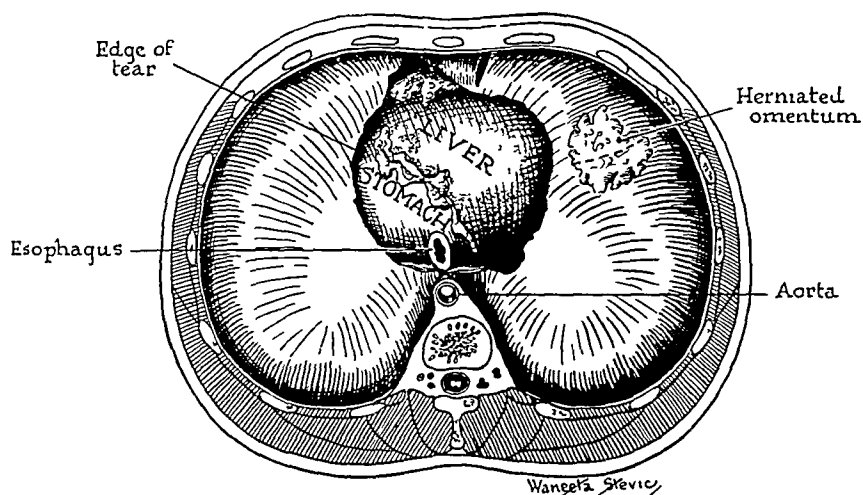


FIG 3—Drawing illustrating the condition of the diaphragm after replacing the herniated abdominal viscera.

Transpleural approach was used in repair of the diaphragm. The important point about this case is that both sides of the chest were wide open at the same time, with simultaneous collapse of both lungs during the operation. Contrary to common belief, the bilateral collapse was not fatal, and the patient had a very smooth anesthesia, which lasted for two hours. As a matter of fact, the anesthetist reported that very little positive pressure was necessary, and that the patient's pulse and blood pressure were remarkably constant. There was less postoperative shock than is generally encountered following extensive intrathoracic operations.

CONCLUSIONS

There are several interesting conclusions to be drawn from this case. In the first place, the decision to defer the operation until the patient was completely over the shock of the accident seemed to be wise. However, since the patient was showing evidence of transient intestinal obstruction it would not have been wise to postpone the operation any longer. The case also illustrates the fact that if intratracheal anesthesia is used it is possible to operate with both sides of the chest open simultaneously, and with both lungs collapsed, without causing undue respiratory embarrassment or an unusual degree of shock. There were two other practical points that are worth mentioning. The first is that the decision to crush the phrenic nerve on the previous day was correct, because having the diaphragm paralyzed made it much

easier to replace the abdominal viscera. Had the nerve not been crushed on the previous day it would have been difficult to have crushed the nerve in its course along the pericardium until after the viscera had been replaced. The final point to mention is that the chest was closed without drainage and,

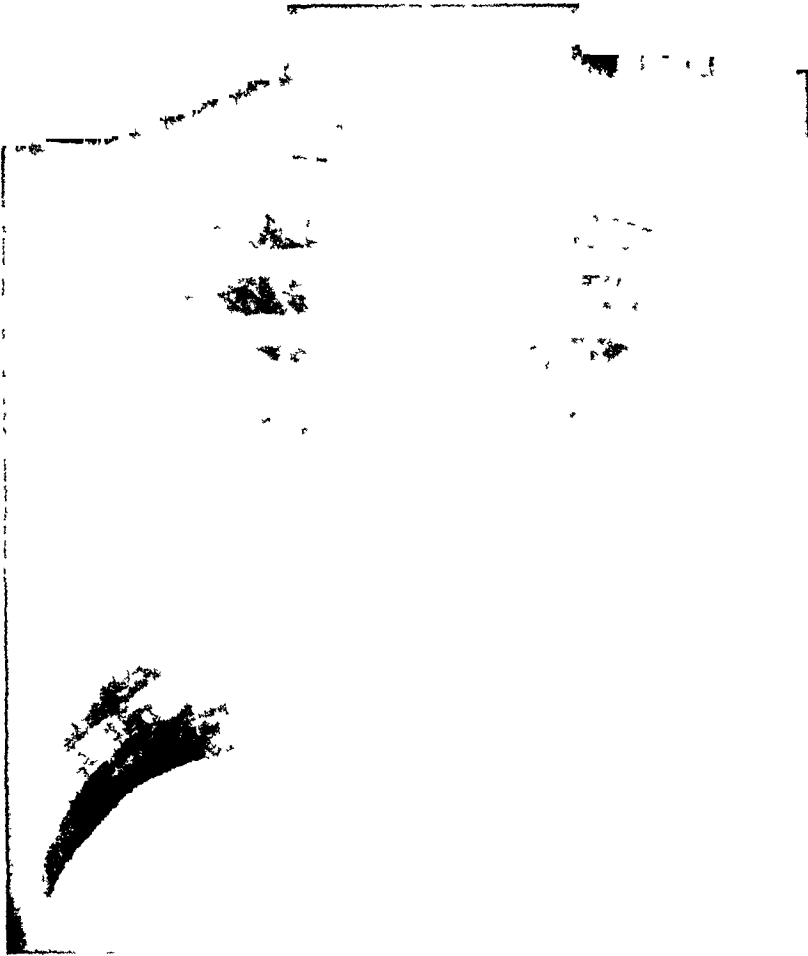


FIG 4—Roentgenogram taken three months after the operation. Healed fractured ribs are shown, also the high position of the paralyzed left diaphragm. There is no evidence of recurrence of the hernia.

while a small amount of fluid formed, no infection was present, and the fluid absorbed spontaneously. No postoperative aspirations were necessary.

REFERENCES

- ¹ Harrington, S. W. Results of Surgical Treatment in 210 Cases of Diaphragmatic Hernia. *Calif and West Med*, 50, 399, June, 1939. *Idem* 51, 27, July, 1939.
- ² Schiffbauer, H. E. Traumatic Hernia-Transpleural Repair. *Calif and West Med*, 50, 180-184, March, 1939.
- ³ Truesdale, P. E. Diaphragmatic Hernia. Report of Cases Illustrating its Varieties. *Southern Surgeon*, 8, 1-2, February, 1939.

TRAUMATIC ARTERIOVENOUS FISTULA

REPORT OF AN UNUSUAL CASE

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AND

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ARTERIOVENOUS FISTULAE, wherever their location may be, always present a challenge to the surgeon as to when to intervene and what procedure to adopt and, finally, how well he can carry out the procedure he deems most likely to afford a favorable end-result in each particular instance

Present-day literature deals fully with the mechanics of production of the abnormal communication between the arteries and vein, as well as describing at great length, the pathologic physiology and surgical procedures in such abnormal communications

In reporting the appended case, it is not the intention of the authors to present any new theories as to the physical, pathologic, physiologic, or surgical aspects of the subject, but merely to report a case somewhat out of the ordinary, which was treated, with a favorable end-result

Case Report—J C D, white, male, age 23, was admitted to Letterman General Hospital, July 25, 1941, with a chief complaint of a thrill and buzzing sensation in his left upper extremity just proximal to the elbow, with each heart beat. Patient stated that approximately eight months prior to admission, while working as a meat-cutter, he accidentally stabbed himself on the medial aspect of the left arm just above the elbow. At the time of the injury blood spurted out as though an artery had been severed. He was treated by a physician shortly after the accident occurred. The bleeding stopped following application of a compression-type bandage, and the wound healed without infection. About one month after the accident occurred he noted, one night, while lying on his left arm, a loud noise occurring simultaneously with each heart beat, and on palpating the area just proximal to the elbow, he could feel a buzzing or thrill. Patient stated that he had no difficulty at any time because of this condition, that he had not noticed any apparent weakness of the left arm, nor had he noticed any evidence of cyanosis or dilatation of the superficial blood vessels. On further questioning, he did admit some shortness of breath on unusual exertion, which, to him, seemed slightly more than he had usually experienced under similar circumstances prior to the injury.

Physical examination was essentially negative, except for a scar, approximately three centimeters long, on the medial surface of the left upper extremity, approximately four centimeters above the elbow. Palpation of this area revealed a sharp systolic thrill, and auscultation elicited a marked bruit, starting in systole and continuing throughout diastole. Blood pressure was 118/65, and was the same in both arms. There was no evidence of venous dilatation distal to the elbow. A diagnosis of an arteriovenous fistula was made, July 31, 1941.

Operation—Under nitrous oxide-ether anesthesia, a six-centimeter incision was made over the brachial artery of the left upper extremity, extending proximally from a point two centimeters above the medial condyle of the humerus. The superficial veins of the anterior surface of the arm were dissected free, and retracted medially and laterally,

TRAUMATIC ARTERIOVENOUS FISTULA

as need be. Immediately beneath this, in the region of the brachial artery, a sharp thrill, originating with the systolic phase of the heart beat, could be felt. By meticulous sharp dissection, a double arteriovenous fistula was isolated (Fig 1). These had occurred between the venae comites and the brachial artery, forming a double "H". The median nerve was retracted medially and the arteries and venous fistula were ligated with No 1 chromic catgut, and then cut. The defects in the brachial artery, both on the

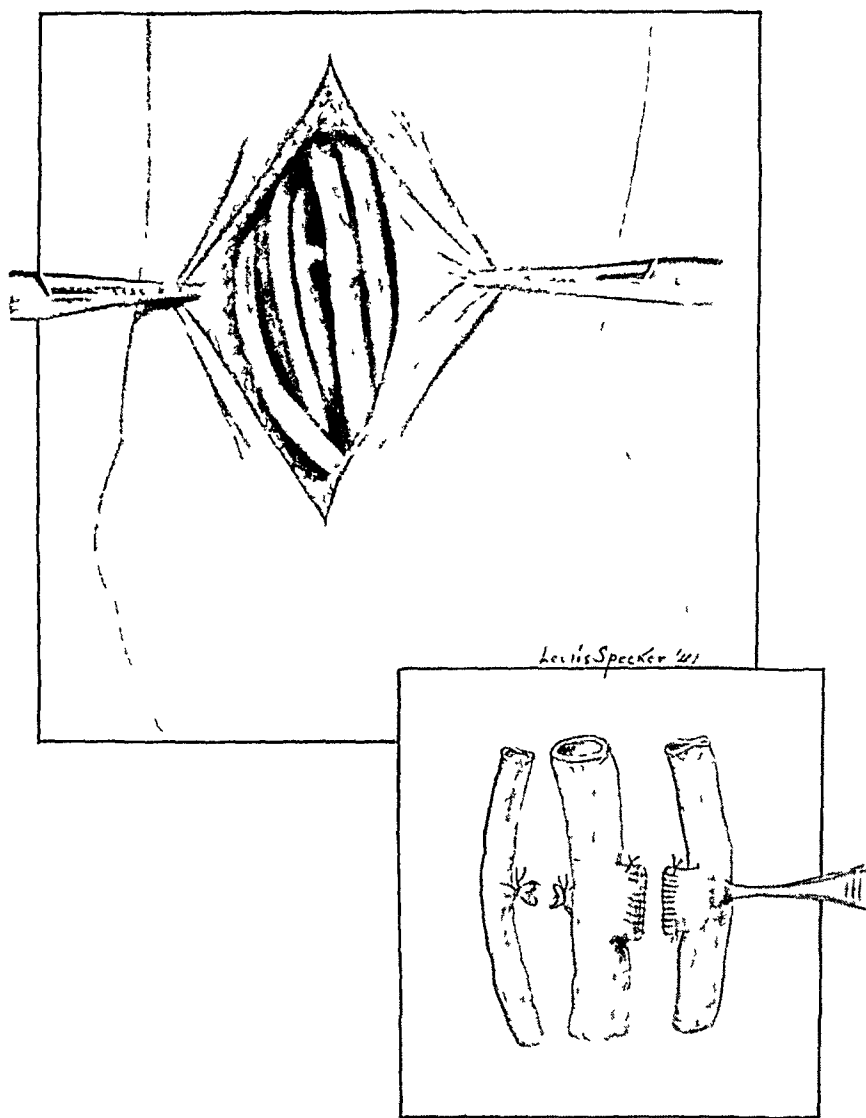


FIG 1—Drawing showing the anatomic relations of the double arteriovenous fistula. Insert: Showing the technic of separation and method of suture.

medial and lateral surfaces, were then repaired by suturing with fine silk (Fig 1). Following this procedure it was noted that the thrill had stopped. Hemostasis was obtained, and the subcutaneous tissues were approximated with a continuous interlocking dermal suture. The arm was put up in extension, with a posterior splint.

The postoperative convalescence was uneventful up to August 25, 1941, at which time he developed an acute upper respiratory infection, which later developed into a mild bronchial pneumonia. This was treated with sulfathiazole, and he became afebrile after three days. On September 5, 1941, sulfathiazole was discontinued, and he was able to

be up and about the ward Examination at this time revealed the wound to be entirely healed, pulse good at the wrist, with no evidence of venous congestion, nor was there any evidence of the thrill or bruit originally heard in the region of the elbow prior to surgery

The patient has fully recovered from the original condition and is to be returned to his duties as a soldier in the near future

HEMANGIOMA OF THE ILEUM

FREDERICK CHRISTOPHER, M D

EVANSTON, ILL

AS HEMANGIOMA of the intestinal tract which comes to clinical recognition is extremely uncommon, it would seem desirable that every case encountered be reported in order to amplify our knowledge of this subject. In 1936, Kaijsei¹ reviewed the literature and found reports of only 74 verified cases of hemangioma of this type. These he classified into five groups. Since then at least 11 additional cases have been reported.

The case described by Pierose² is particularly instructive. The patient had had symptoms for 15 years, and it was only after much study and at

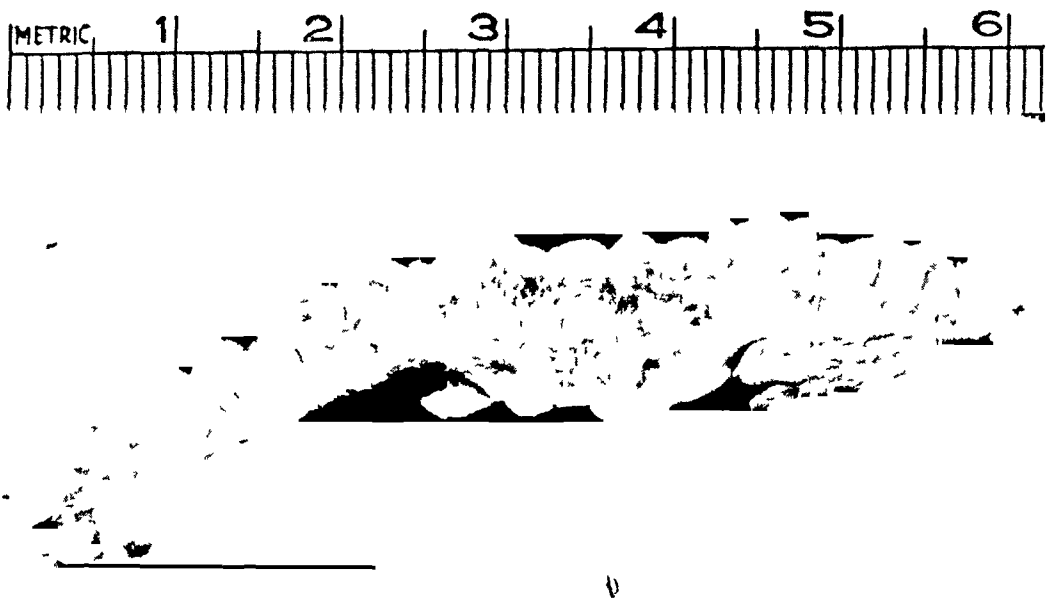


FIG 1—Gross appearance of hemangioma of the ileum

the third celiotomy that a correct diagnosis was made and the lesion resected, with recovery of the patient. It is well to emphasize Pierose' statement that "when a patient experiences repeated attacks of melena which cannot be explained by a thorough study of the history, physical manifestations and laboratory examinations, the possibility of hemangioma of the gastrointestinal tract should always be considered." Another interesting case, that of a boy, age 12, was recently reported by White³. In this case severe hemorrhage from the rectum had suggested the diagnosis of a bleeding ulcer of a Meckel's diverticulum. At operation, the "last six inches of the ileum and ileocecal junction were much thickened and infiltrated by masses of tortuous, engorged blood vessels." The patient recovered after resection of the terminal ileum and cecum.

Recently I operated upon a patient with hemangioma of the ileum, the data in this case being as follows

Case Report—B S, female, age 26, was admitted to the Evanston Hospital, April 30, 1941, because of recent attacks of faintness and breathlessness. The history was otherwise negative. There had been no tarry stools. With the patient recumbent, the blood pressure in the right arm was 80/52, in the left arm it was 110/70. A loud systolic murmur was noted. On May 1 the blood count showed Hb 42.2 per



FIG 2—Microscopic appearance of hemangioma of the ileum showing the point from which the hemorrhage occurred

cent, RBC 2,160,000, WBC 10,250. On May 3 the count showed Hb 35.7 per cent, RBC 1,830,000, WBC 11,900. Blood cultures and urinalysis gave negative results. The stools showed 4-plus blood, gross and occult, on four examinations. No blood was found in the stomach contents. An electrocardiogram was normal. Four blood transfusions were administered, and on May 23 the blood count showed Hb 68.1 per cent, and RBC 3,620,000. The patient was discharged on that day, with a diagnosis of gastro-intestinal hemorrhage of undetermined origin, possibly due to a Meckel's diverticulum. She was to follow an ulcer diet.

On June 9 the patient was readmitted. The blood count showed Hb 81.1 per cent, RBC 4,150,000, WBC 7,850. Roentgenologic examination of the gastrointestinal tract revealed no abnormality, and the patient was discharged on June 11. She was readmitted on June 22, with complaints of fatigue and dizziness. Blood was found in the stool. The red blood cell count and the hemoglobin value declined steadily and on June 28 were 26.0 per cent and 1,410,000, respectively. Transfusions were administered on June 22 and July 2, 5 and 7. On July 7 the hemoglobin value was 38.9 per cent, and the red blood cell count was 1,830,000.

Operation—July 8, 1941. The abdomen was opened through a long right rectus incision. No Meckel's diverticulum was found. As far as could be ascertained by palpation and inspection, the stomach, duodenum and large and small bowel were normal, save for a lesion about the junction of the jejunum and ileum. At this point, on both sides of the intestine at the mesenteric border, there was a strikingly bright red coloration. This area was irregular in contour and slightly granular, with a smooth serosa. On one side of the bowel the lesion measured about 1 x 2 inches, and on the other side about $\frac{1}{2}$ x 1 inches. Opposite it were several small, shotty nodes in the mesentery. Four inches of the small bowel was resected, and an end-to-end anastomosis was established. The patient had an uneventful convalescence, and left the hospital on July 24. Two months later she was able to ride horseback.

Pathologic Examination—Gross. Dr. E. L. Benjamin. The resected segment of the ileum is 7 cm long and 5 cm in circumference. The serosal surface presents a triangular, dark red, slightly granular area. Its base, 1.5 cm long, arises from the mesenteric border. It is 2 cm long and its hypotenuse measures 21 Mm. A similar lesion, although slightly smaller, arises from the mesenteric border on the opposite surface of the bowel. The opened bowel displays a roughly round, dark red area, corresponding to the position of the mesentery involved in the above-mentioned lesion. The mucosal lesion measures 21 by 20 Mm. Its borders are slightly irregular, and, except for a slightly eccentrically placed, soft, gray area, 3 cm in diameter and 1 Mm high, the mucosa is normal (Fig. 1). *Microscopic Diagnosis*. Congenital hemangioma of the ileum, with secondary ulceration and hemorrhage (Fig. 2).

REFERENCES

- ¹ Kayser, R. Arch. f. klin. Chir., 187, 351 and 661, 1936.
- ² Pierose, P. N. J. A. M. A., 115, 209, 1940.
- ³ White, R. J. South. Surgeon, 10, 886, 1941.
- ⁴ Brown, A. J. Surg., Gynec. & Obst., 39, 191, 1924.
- ⁵ Hunt, V. C. Tr. West. S. A., 1940, p. 440.

MALIGNANT TERATOMA OF THE ARM

CASE REPORT

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THE FOLLOWING CASE is presented to illustrate some of the difficulties which face the physician in making a correct diagnosis. Presence of a malignant teratoma in this case was not suspected, and diagnosis of a rare disease, one must assume, is often merely a question of thinking of it as a possibility.

Case Report—The patient, white, male, age 49, was admitted to the State Institute for the Study of Malignant Diseases, July 3, 1940, complaining of a tumor mass of the left arm. He stated that about 25 years ago he noticed a small lump on his left upper arm. It had increased in size gradually until about one and one-half years ago, when it began to grow very rapidly. At the time of his admission it was as large as a medium-sized orange, felt somewhat hard, and had a dark purplish hue. About 20 days previously it broke on the surface, and there was a slight bloody discharge. Six days ago it broke again, and there was some pus and bloody drainage. During the past five or six days there has been some muscle pain but no other distressing symptoms.

Physical Examination—This was essentially negative except for the tumor mass, which involved the left arm just above the elbow. It was located on the dorsal surface and about the insertion of the deltoid muscle, somewhat oval in outline, and measured about 14 cm in diameter. It was partially ulcerated on the surface and held to subcutaneous tissues by a narrow pedicle. It was freely movable and of semifirm consistency, with the superficial veins markedly dilated. The laboratory and roentgenologic findings were negative. *Provisional Diagnoses*: Lipoma, fibrolipoma or sarcoma.

Operation—Under 0.5 per cent novocain anesthesia, an elliptical incision was made. The skin flaps were undermined to some extent down to the deep fascia, which was involved, but the muscular layer was free of any involvement. The tumor was well encapsulated but it had perforated through the capsule and had undergone partial central and surface necrosis. Small areas of cystic degeneration were also present. The tumor was removed *in toto*, and the skin approximated by three retaining linen sutures and skin clips. A small gauze drain was inserted.

Pathologic Examination—Dr A. A. Thibaudeau. Section of tumor from the left arm shows a growth composed largely of small round and spindle cells disposed about blood vessels. In these areas the histologic picture is that of a tumor arising from mesoblastic cells. Due to the characteristic disposition of the cells about blood vessels and their general histologic characteristics, the picture in these areas is that of an endothelioma. However, in some areas, islands of squamous epithelium of anaplastic type with marked variation in size, shape, and staining quality of cells, and with some pearl formation are found in the areas above described (Figs 1 and 2). This squamous epithelium lies deep below the skin surface and has evidently no connection with it. Large areas of fibrosis and necrosis are seen about the edges of the growth. *Pathologic Diagnosis*: Malignant teratoma.

Postoperative Course—The patient's recovery, postoperatively, was uneventful, and he was discharged on the day of operation, to return to the Out-Patient Clinic for

MALIGNANT TERATOMA OF ARM

additional care and dressings. The wound healed completely in 12 days. A course of high voltage roentgenotherapy was given over the affected area of the arm within two weeks after operation, because of the pathologic report of malignant teratoma. Two fields were chosen, one anterior and the other posterior, and daily doses, to a total of 3,564 r to each field, were given. This patient is well today with no recurrence, and has resumed his former occupation.

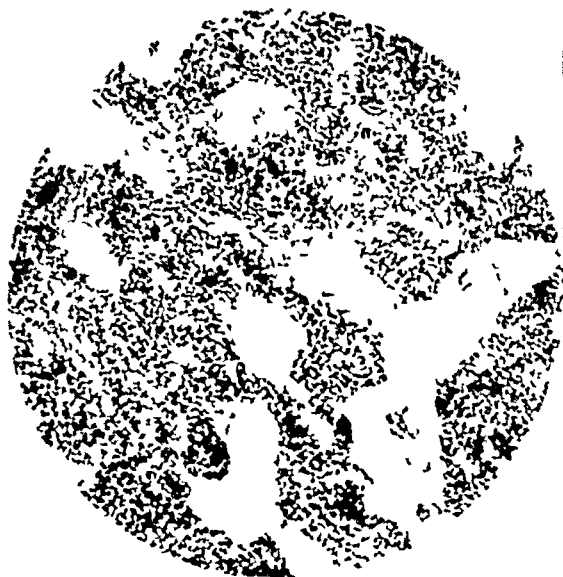


FIG 1—Showing cells of the mesoblastic layer, together with masses of cells of epidermal origin



FIG 2—Showing masses of cells of mesoblastic origin, arranged about blood vessels

COMMENT—Malignant teratoma is probably not a rare occurrence, but malignant teratoma of the upper extremity must be regarded as unusual. The cause of malignant teratoma is not definitely settled.

This case furnishes a striking demonstration of the value of the histologic examination of any new growth removed at operation. By this diagnostic procedure a correct diagnosis was made and the proper postoperative roentgenotherapy was administered.

CLAVICLE FRACTURE TREATED WITH SKELETAL TRACTION

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CLAVICLE FRACTURES are not usually considered serious because of their facility in healing despite the inaccuracy of reduction. Many forms of treatment have been employed, no one of which has been satisfactory from all considerations—comfort, accurate reduction, early healing, and final cosmetic

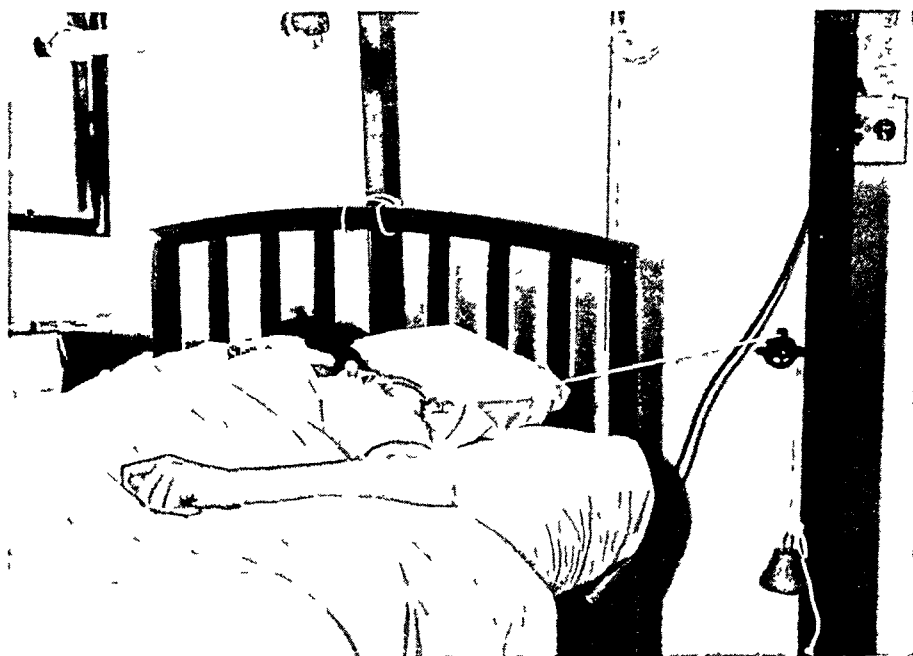


FIG 1—Skeletal traction to outer end of clavicle

result. With the usual inaccurate replacement of the fracture fragments, healing is attended by a large mass of unsightly callus. Also, in the few cases where open reduction is undertaken, the scar must, necessarily, be placed in an exposed position.

The suitability of using skeletal traction, with a small wire through the outer end of the clavicle, to obtain reduction, union, and good cosmetic result was obtained in the cases herewith, reported.

Case 1—In this instance a small incision for placement of the wire was made, under general anesthesia. A clevis was applied, with five pounds traction, to a floor frame, and the patient was placed supine in a standard hospital bed, with the head of it

FIG 2



FIG 3

FIG 2—Original roentgenogram of clavicle with overlapping of fragments

FIG 3—Roentgenogram three weeks after fracture, showing reduction and callus formation

slightly elevated (Fig 1) After 24 hours the fracture had become reduced and slightly overpulled (Figs 2 and 3), so the weight was decreased to three pounds Three weeks after the fracture, callus was apparent both clinically and roentgenographically

Case 2—The patient, a female, age 12, had previously sustained a fracture of the clavicle, which was treated by figure-of-eight bandage, three weeks later, she fell and caused a refracture through the callus, with overlap of the fragments This was treated, similarly to Case 1, by skeletal traction, with satisfactory reduction

The convalescence was much more comfortable, and uneventful, than by any other method of treatment previously employed, and a functionally and cosmetically satisfactory end-result was obtained

THE SO-CALLED "COMMON ILIAC VEIN" OF THE RABBIT

DELL THEODORE LUNDQUIST, M D

PALO ALTO, CALIF

FOURTEEN YEARS AGO, after doing a short series of experiments on rabbits, ligating the common iliac artery, with and without its accompanying vein, I decided not to submit the work for publication, because it seemed that the anatomic relations were such that the results could not be carried over to the human. In short, reference to published anatomies of the rabbit,^{1, 5, 7} confirmed by my observations *in vivo*, at autopsy, and after stereoroentgenography of the venous system following injection with Hill's mass⁶ (which was facilitated by first perfusing the arteriovenous system with "normal" saline made with tap water) all led to the conclusion that the rabbit has no bilateral common iliac vein. It has a "trifurcation" of the vena cava inferior made up of a single common internal iliac and the right and left external iliacs. The common internal iliac vein is formed by the junction of the right and left internal iliacs.

Therefore, those who have reported ligating the common iliac vein of the rabbit have doubtless ligated only the external iliac. Recent reference to the literature has shown that this mistake is still extant, hence the perpetration of this report to end the perpetuation of an error, and to erect a sign "Blind Alley."

The late Dr Emmett Rixford called to my attention one of the earliest pieces of work done by Cooper³ on experimental ligation of arteries with and without the accompanying veins, also reporting an operative case, where the surgeon was compelled to ligate the vein, as well as the artery (external iliac) and was surprised at the results. His experiments were on dogs. He referred to a surgical hope of successful gradual retroperitoneal occlusion of the aorta.

Whether the anatomy of the sympathetic nervous system of the rabbit is different from the human is a question that might be investigated in connection with the various results reported. In fact, whether the operations of venous and arterial ligations accomplish part of their effects through the sympathetic nerves affected by the ligations might well be asked.

The unsuitability of the rabbit for work involving temperature readings unless an average for each one is established is attested by Scott and Simon.⁸

BIBLIOGRAPHY

(The full list of references to those who have fallen into this error is not appended—most of them are included in references of Gage and Ochsner,³ and of Brooks, Johnson and Kirtley²)

¹ Bensley, B. U. Practical Anatomy of the Rabbit. Toronto: The University Press, 1910, Pages 133, 134.

- ² Brooks, Barney, Johnson, George S, and Kirtley, James A Simultaneous Vein Li-
gation Surg, Gynec and Obst, 59, 496-500, September, 1934
- ³ Cooper, E S On Ligating the Satellite Veins in Connexion with the Arteries which
they Accompany Calif Med Jour, 1, 441, April, 1857
- ⁴ Gage, Mims, and Ochsner, Alton Prevention of Ischemic Gangrene, *etc* ANNALS
OF SURGERY, 112, 938-959, November, 1940
- ⁵ Gerhardt Das Kaninchen (Klinkhardt, pub) Leipzig, 1909 Page 254
- ⁶ Hill, E C Notes on an Opaque X-ray Mass Johns Hopkins Hosp Bull, 35,
208, 1924
- ⁷ Krause, W Anatomie des Kaninchens Zweite Aufl, Engelmann, Leipzig, 1884
Pages 276, 277
- ⁸ Scott, J M, and Simon, C E The Thermic and Leukocytic Response of the Rabbit
to Inoculation with the Virus of Measles Am Jour of Hygiene, 4, 559, Sep-
tember, 1925

A NEUROSURGICAL HEAD-REST

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A HEAD-REST for supratentorial craniotomies, as satisfactory as the Adson frame in cerebellar approaches, has been a problem for which we offer the following simple, stable device as a solution

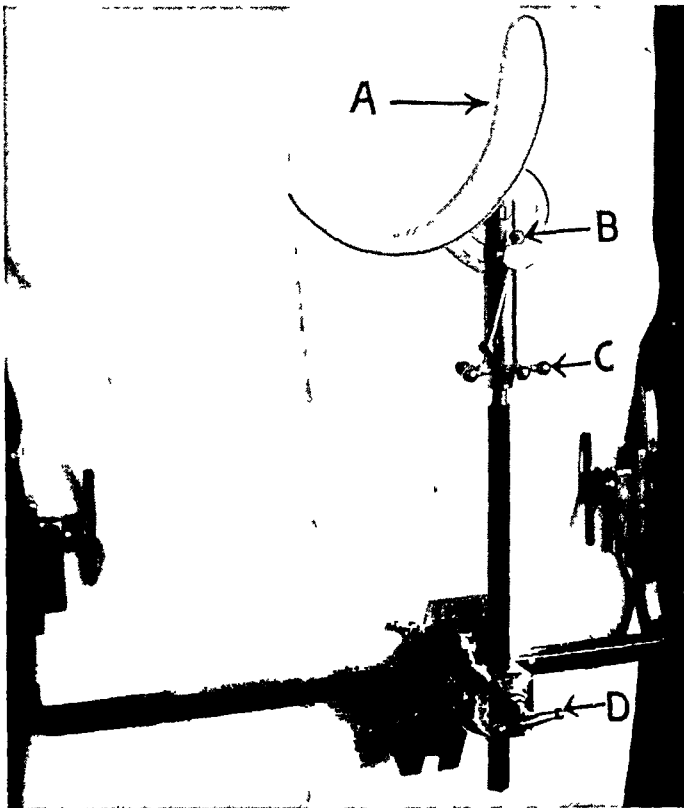


FIG 1—The head rest attached to the cerebellar frame

The head-rest of a regular Adson cerebellar frame is removed and the following apparatus is attached to the frame A is the unpadded head-support which extends from just beyond the occipital region along the side of the head and face It can be seen that the frontal, temporal, parietal and part of the occipital regions are readily accessible By changing the padding it is a simple matter to fit it to different size heads The view of the head in the vertical position would lead one to believe that the head might easily slide out of the support The drappings, the weight of the head, and the fact that the surgeon is working from the opposite side prevents any

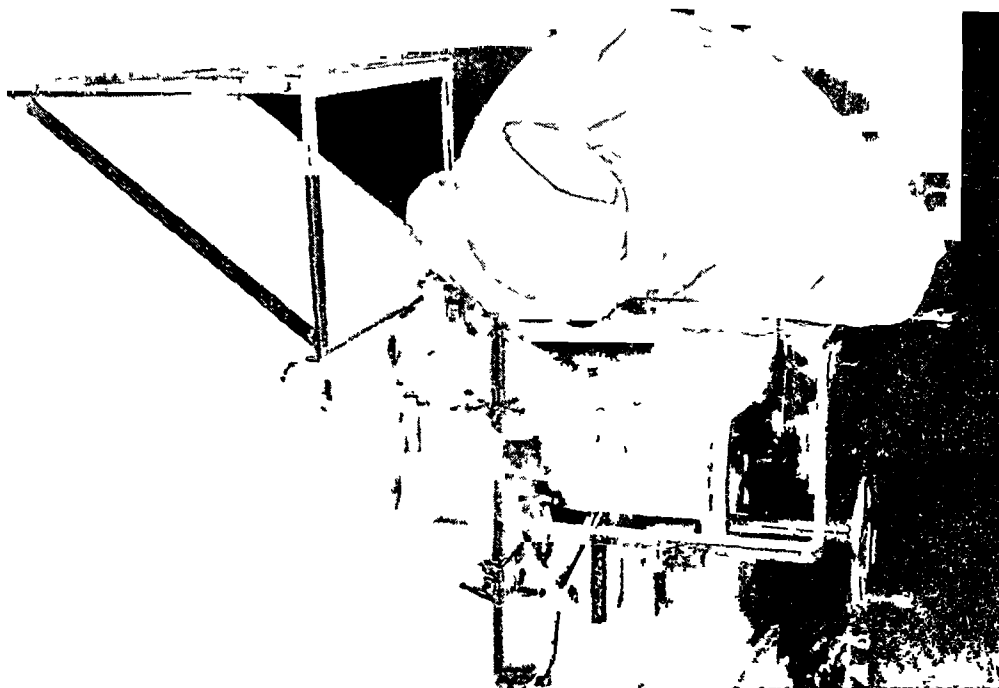


FIG 2—Head in the oblique position (The anesthetist's frame is attached to the table)

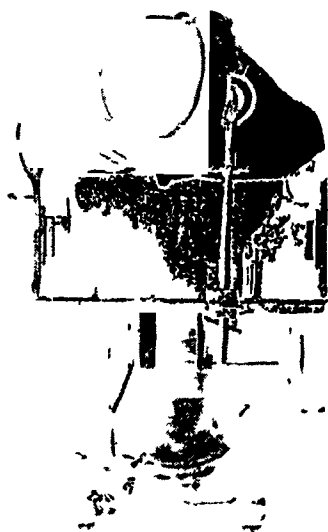


FIG 3—The head in the vertical position



FIG 4—The head in the lateral position, right side up

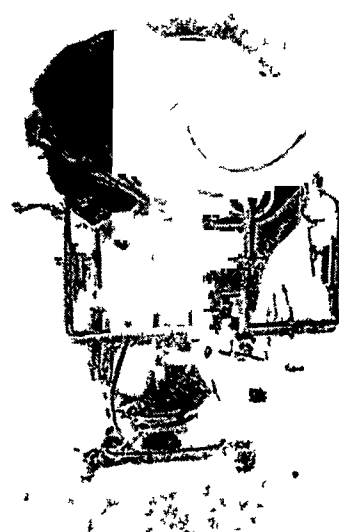


FIG 5—The head in the lateral position, left side up

possibility of this occurring B Is an adjustable device used to hold the head-support at any angle from a lateral to a vertical position If the surgeon desires the angle of the head to be changed during the operation, this can be done readily by the anesthetist When C is loosened the head-rest can be turned for either a right or left approach D Is a screw that allows the head-rest to be raised or lowered At D this apparatus is to be inserted in place of the ordinary cerebellar rest

The frame, beneath which the anesthetist sits, is supported by a bar which can be readily attached to the operating table It gives sufficient room for the anesthetist to watch the patient without interfering with the operator or assistants

We have been using this apparatus for supratentorial craniotomies for the past few months with satisfactory results

AN EXPANSION REAMER

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THE PREPARATION of the acetabulum in performing an arthroplasty of the hip joint is a major feature of the operation. In any type of ankylosis of the hip, and especially in the bony variety, a variable degree of reaming of the acetabulum is required to obtain a roomy and adequate socket for the newly constructed femoral head. Chisels of various sizes and shapes are used to break up the ankylosis and to enucleate enough bone from the side of the pelvis to establish a depression which is the beginning of an acetabulum. One then proceeds to deepen and shape the acetabulum and to obtain a comparatively smooth articulating surface by means of a reamer. The Doyen reamer is the most popular instrument for this purpose, and it is indeed very useful, but in its frequent use I have found three faults. First, the Doyen reamer creates a cavity of a given size, and it is usually necessary to use three reamers of increasing size to obtain a large enough acetabulum. The large reamer cannot be used at once because the depression made in the pelvis by the chisels is not big enough to admit it. Hence, three different instruments have to be inserted into the wound. Second, the cutting edges of the Doyen reamer are not very strong and are so placed that only a very small quantity of bone is removed in one revolution, therefore, the surgeon has to expend a great deal of energy in taking out an adequate amount of bone, especially if it is sclerosed, from the sides of the acetabulum. Third, the reamer is operated by turning its distal bulbous end, this is often very difficult because the moisture of the wound makes the instrument slippery, and, despite the fact that one uses gauze, a laparotomy pad or a towel to grip the instrument, it can be rotated only by the use of much force.

The above experiences and considerations led me to devise an expansion bone reamer based on the principle of the expansion bit used in carpentry. The cutting edges of my instrument are very strong and are easily and gradually separated, while the instrument remains in the wound, permitting the surgeon to enlarge the new acetabulum to the required size. In addition, a handle attached to the distal part of the reamer facilitates its operation and avoids the necessity of the use of much force.

The instrument (Fig 1) is all metal, and can be sterilized by boiling. It consists of three curved, strong knives (Fig 2) of surgical steel, mounted through joints (Fig 3) on a steel rod, which lies inside of a fenestrated cylinder of seamless steel tubing and projects beyond the cylinder by a threaded extremity, on to which fits a controlling knurled knob (Fig 5 B). The knurled knob is used to change and regulate the relative position of the rod in the cylindrical housing, and thus separate or approximate the knives

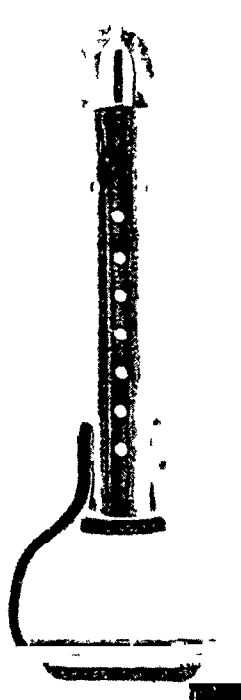


FIG 1

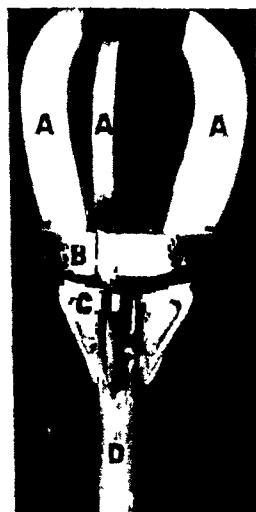


FIG 2



FIG 3



FIG 4

FIG 1—Showing the assembled instrument with the blades closed. The diameter of the surface which the blades cut in this position is $1\frac{3}{8}$ inches. The fenestrations in the cylindrical case not only lighten the weight of the instrument but permit thorough cleansing.

FIG 2—Showing the three cutting blades, the guide ring and pins, and the rod with the expansion head at one end and the thread at the other end.

FIG 3—An enlarged view of the blades and expansion head on the rod. (a) Knives (b) Guide ring (c) Expansion head (d) Rod.

FIG 4—Assembled instrument with knives open to diameter of $2\frac{1}{4}$ inches.

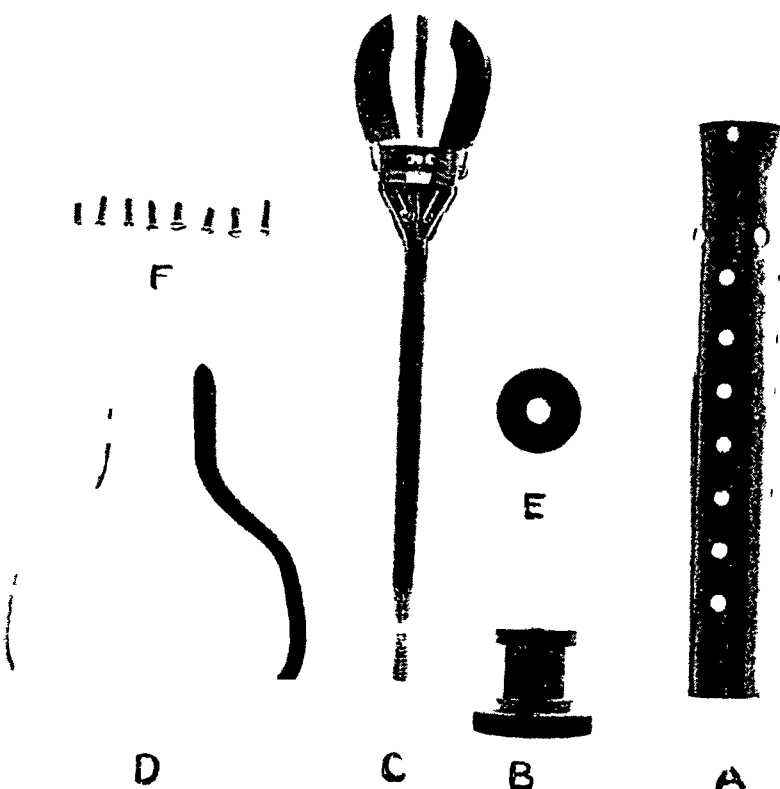


FIG 5—Instrument taken apart. (A) Cylinder (B) Knurled knob (C) Rod with blades (D) Handle (E) Small ring to cap upper part of cylinder, allowing rod to pass through it (F) Eight screws to secure the various parts to the cylinder.

projecting beyond the opposite end of the cylinder. To the cylindrical case is attached a fairly large handle of duraluminum (hence, very light in weight) by which the instrument may be easily rotated. The blades when closed (Fig 1) have a diameter of $1\frac{5}{8}$ inches, and when open (Fig 4), a diameter of $2\frac{1}{4}$ inches, thus giving one an adequate range for the construction of any adult acetabulum. The weight of this reamer is only $1\frac{1}{2}$ pounds. The cylindrical case, the rod and the blades are made of steel, but the handle, the guide-ring and the knurled knob are of duraluminum.

The expansion reamer described was designed in the brace shop of the Hospital for Joint Diseases, with the kind and enthusiastic assistance of Mr Jack Schwartz and Mr Gaston Heitz, to both of whom I am very deeply indebted. I have used the instrument and find it to have the following advantages:

- (1) It is light in weight, but strong.
- (2) An acetabulum may be reamed out to the desired size by extending the cutting surfaces of the knives, without removing the instrument from the wound.
- (3) By means of the large handle, rotation of the reamer can be performed with but slight effort.
- (4) The position of the cutting blades, and hence the size of the new acetabulum, is easily regulated by the knurled knob.

BOOK REVIEW

CHINA'S HEALTH PROBLEMS By Szeming Sze, M A, M B B Ch (Cantab), New York City China Institute in America, Inc 1942

A REMARKABLE MONOGRAPH by Szeming Sze on China's Health Problems has had its first printing in July of this year by the China Institute in America, which deserves a careful reading by Americans at this time

That there is a problem is evidenced by his statements that there is at the present time a morbidity of sixteen millions a day, and a mortality of ten millions a year, of which, it is conceded, four millions are unnecessary

To meet this responsibility, available medical facilities are meager and the distribution of them uneven In the whole country there are but ten thousand doctors and thirty-eight thousand hospital beds Based upon American standards, and with the same morbidity, China should have two hundred and sixty thousand physicians and two million hospital beds But this again should be doubled, as the incidence of disease in China is more than twice that of the United States

To meet this stupendous problem he suggests State Medicine as the only answer for the 85 per cent of the population who live in the rural districts He accepts the plan which has been in operation in Scandanavia for many years, in which a network of health centers are grouped around a series of Provincial Hospitals, and all controlled by a National Health Administration That such a plan, known as "The New Hsien System" has been functioning in China for some time is evidenced by the report of the Director of the National Health Administration for 1940

It is necessary for one to meticulously read this presentation of Szeming Sze to appreciate the grasp the author has upon this amazing problem His discussion, in a series of chapters devoted to health, medical education, the Army Medical Service and Civilian Medical Relief are recommended to our medical profession and Government authorities during these times of change and adjustment

Not only do we recommend it, but regard it as compulsory reading for the Profession and general public

WALTER ESTELL LEE

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INDEX TO VOLUME 116

A

- Abscess of the Liver due to Anaerobic Nonhemolytic Streptococcus, Primary, 217, Pulmonary, 373
- ACKMAN, DOUGLAS A Practical Concept for the Treatment of Major and Minor Burns, 641
- Adamantinoma, Hemisection of the Mandible for Recurrent, 277
- Adenolymphoma of the Parotid Gland, 43
- Adrenal Associated with Hypertension, Adrenalin Producing Pheochromocytoma of the, 54
- Adrenalin Producing Pheochromocytoma of the Adrenal Associated with Hypertension, 54
- ALTEMEIER, W A Cysts of the Spleen, 98
- Amputation, Spontaneous, 155
- Anatomic Approach to Pulmonary Resection, 782
- Anesthesiology, Posterior Pituitary Extract in, 898
- Aneurysm, Arteriovenous, Involving the Left Innominate Vein and the Left Common Carotid Artery, Successful Closure of an, 700, Complicated Case of, Involving the Iliac and Femoral Arteries, 708
- Announcement of Fellowships in Medicine and Public Health, 597
- Appendicitis Operations, Drainage and Wound Closure Technique in, 435
- ARIEL, I Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract, 924
- Arm (Right) Thrombosis and Gangrene of, Associated with Polycythemia Vera Its Relation to "Effort Thrombosis," 184, Lymphedema of the, Following Radical Mastectomy for Carcinoma of Breast, 816, Malignant Teratoma of the, 948
- Arteries, Femoral and Iliac, A Complicated Case of Aneurysm Involving the, 708
- Arteriovenous Fistula, 470
- Artery, Left Common Carotid, Successful Closure of an Arteriovenous Aneurysm Involving the Left Innominate Vein and the Left Common Carotid, 700, Occlusion of the Portal Vein and Hepatic, 833
- Astragalus, Less Common Lesions of the, 891

- ATLAS, LAWRENCE N A Complicated Case of Aneurysm Involving the Iliac and Femoral Arteries, 708, Sympathetic Denervation Limited to the Blood Vessels of the Leg and Foot, II, 476
- Atraumatic Fascial Suture Needle, 315
- Atresia of the Duodenum, 334, Of the Small Intestine, Multiple, 337
- AUCHINCLOSS, HUGH Drainage and Wound Closure Technique in Appendicitis Operations, 435

B

- BABCOCK, W WAYNE Temporary Occlusion of the Portal Vein and Hepatic Artery, 833
- Bacteriology of the Common Bile Duct in Comparison with the other Extrahepatic Segments of the Biliary Tract, A Study of the, 360
- BALKIN, RUTH B Adrenalin Producing Pheochromocytoma of the Adrenal Associated with Hypertension, 54
- Barbiturates, A Study of the "Shock Delaying" Action of the, 658
- BECK, CLAUDE S An Intrapericardial Teratoma and a Tumor of the Heart, Both Removed Operatively, 161
- BEECHER, HENRY K A Study of the "Shock Delaying" Action of the Barbiturates, 658
- BELLIS CARROLL J A Punch for Cutting Cottonoid Sponges for use in Neurosurgical Operations, 318
- BFRGER, LOUIS Primary Carcinoma of the Duodenum, 738
- BERRY, FRANK B Cardiocirculatory Dynamics in Surgical Shock, 127, The Effect of Pneumonecctomy upon Cardiopulmonary Function in Adult Patients, 532
- BETTMAN, RALPH B Cholecystectomy without Drainage, 928
- Biliary Tract, A Study of the Bacteriology of the Common Bile Duct, in Comparison with the other Segments of the, 360
- BLADES, BRIAN The Anatomic Approach to Pulmonary Resection, 782
- Blood, Observations of the Failure of Heparin to Inhibit the Clotting of, (*in vitro* by Staphylococci), 430

- BLOTNER, CARL Sliding and other Large Bowel Herniae, 394
- BLUM, LESTER The Use of Myotomy in the Repair of Divided Flexor Tendons, 461
- BOOK REVIEW A Manual of the Treatment of Fractures, Reviewed by Walter Estell Lee, 320, China's Health Problems, Reviewed by Walter Estell Lee, 960, Intestinal Obstruction, Reviewed by Walter Estell Lee, 640
- BOOKS RECEIVED 800
- BRAUND, RALPH Sacrococcygeal Teratoid Tumor, 76
- Brazilian Congress of Orthopedics and Traumatology, The Fifth, 480
- Breast, Carcinoma of the, 801, Lymphedema of the Arm following Radical Mastectomy for Carcinoma of, 816
- BREIDENBACH, LESTER The Stader Reduction Splint, 623
- BREWER, LYMAN A Chest Injuries, 668
- Bronchus, Closure of the, Following Total Pneumectomy, 481
- BURCH, JOHN C An Experimental Approach to the Problem of Menstrual Disorders, 604
- Burns, Immediate Skin Grafting in the Treatment of, 445, Major and Minor, A Practical Concept for the Treatment of, 641
- BURTON, CLAUDE C Sliding and other Large Bowel Herniae, 394
- BUSCHENHENKE, GERARD A Neurosurgical Head rest, 954
- C**
- Calcified Unilocular Cyst of the Spleen, 933
- CAMPBELL, ELDRIDGE Studies on the Use of Metals in Surgery, Part II, 763
- Cancer of the Cervical Esophagus, 86, of the Gastrointestinal Tract, Metabolic Studies in Patients with, 924, of the Rectum, Urologic Complications of, 6, Carcinoma of the Breast, 801, Of Breast, Lymphedema of the Arm following Radical Mastectomy for, 816, Of the Cervix Uteri as a Cause of Pathologic Central Dislocation of the Hip, Invasion of the Bony Pelvis by, 1, Of the Cystic Duct, Common Duct Obstruction Due to Primary, 141, Of the Duodenum, Primary, 738, Of the Rectum, The Lymphatic and Venous Spread, 200
- Cardiocirculatory Dynamics in Surgical Shock, 127
- Cardiopulmonary Function in Adult Patients, The Effect of Pneumectomy Upon, 532
- CAYLOR, HAROLD D Arteriovenous Fistula, 470
- CHAFEE, JOHN S Postmortem Peritoneoscopy, 843
- Chest Injuries, 668
- CHILD, CHARLES G Noninfective Gangrene Following Fractures of the Lower Leg, 721
- CHINA'S HEALTH PROBLEMS, 960
- Cholecystectomy with Drainage, 928
- CHRISTOPHER, FREDERICK Hemangioma of the Ileum, 945
- CHRISTY, C J Malignant Teratoma of the Arm, 948
- CHURCHILL, EDWARD D Transthoracic Resection of Tumors of the Esophagus and Stomach (Case Reports), 566
- CLAMMER, GEORGE R Atresia of the Duodenum, 334
- Clavicle Fracture Treated with Skeletal Traction, 950
- Closure of the Bronchus Following Total Pneumectomy, 481
- Colon and Rectal Surgery, The Increasing Usefulness of the Devine Colostomy in Left, 913
- Common Duct Obstruction Due to Primary Carcinoma of the Cystic Duct, 141
- Comparison of the Results of Roentgen Rays, Sulfanilamide and Serum Therapy in Experimental Gas Gangrene in the Pigeon, 713
- Complicated Case of Aneurysm Involving the Iliac and Femoral Arteries, 708
- Compresses, The Use of a Lamp to Warm Moist, 776
- Control of Hair and Feather Pigmentation as Revealed by Grafting Melanophores in the Embryo, 598
- COOPER, FREDERICK W, JR Immediate and Late Results of Perforation of Peptic Ulcer, 194
- COURNAND, ANDRE The Effect of Pneumectomy upon Cardiopulmonary Function in Adult Patients, 532
- COX, MARCUS E Myoepithelial Hamartoma of the Ileum with Intussusception, 355
- Cruveilhier Baumgarten Syndrome (Splenomegaly, Portal Hypertension and Patent Umbilical Vein), 860
- Cyst of the Liver, Solitary Nonparasitic, 751, Peritonitis Due to Perforation of an Infected Urachus, 154, Of the Spleen, Calcified, Unilocular, 933, Of the Spleen, Hemorrhagic, 103
- Cystostomy, Siphon Drainage for Superapubic, 159
- Cysts, Pilonidal, and Sinuses A Method of Wound Closure, 687

D

- Denervation Limited to the Blood Vessels of the Leg and Foot, Sympathetic, 476
- DENNEEN, EDWARD V Hemorrhagic Cyst of the Spleen, 103
- Devine Colostomy, The Increasing Usefulness of, in Left Colon and Rectal Surgery, 913
- Dislocation of the Hip, Invasion of the Bony Pelvis by Carcinoma of the Cervix Uteri as a Cause of Pathologic Central, 1, Of the Lower End of the Ulna, So called, 282
- DOBZANIECKI, WLADYSLAW Meningocele Spinalis Traumatica Spuria, 150
- DOLLEY, FRANK S Chest Injuries, 668
- DOWDLE, EDWARD Multiple Primary Nonspecific Jejunal Ulcers, with Chronic Duodenal Dilatation, 348
- Drainage and Wound Closure Technique in Appendicitis Operations, 435
- DUCKETT, J W Intestinal Obstruction in the Newborn, 321
- Duct, A Study of the Bacteriology of the Common Bile, in Comparison with the other Extrahepatic Segments of the Biliary Tract, 360, Obstruction Due to Primary Carcinoma of the Cystic Duct, Common, 141, Spontaneous Rupture of a Normal Hepatic, 137
- Duodenal Dilatation, Chronic, Multiple, Primary, Nonspecific Jejunal Ulcers with, 348, Tumor of Unusual Character, 864
- Duodenum, Atresia of the, 334, Primary Carcinoma of the, 738

E

- Effect of Pneumonectomy upon Cardiopulmonary Function in Adult Patients, 532
- "Effort Thrombosis," Its Relation to Thrombosis and Gangrene of Right Arm associated with Polycythemia Vera, 184
- ECER, SHERMAN A Spontaneous External Biliary Fistula, 931
- EISAMAN, JACK L Arteriovenous Fistula, 470
- LITZEN, OLIVER Multiple Atresia of the Small Intestine, 337
- ELDER, J R Invasion of the Bony Pelvis by Carcinoma of the Cervix Uteri as a Cause of Pathologic Central Dislocation of the Hip, 1
- Electroencephalographic Diagnosis of Subdural Hemorrhage, 452
- ELAELES, GERARDO A Study of the Bacteriology of the Common Bile Duct in Comparison with the other Extrahepatic Segments of the Biliary Tract, 360

- Embolism, Recent Experiences with Thrombophlebitis of the Lower Extremity and Pulmonary, 574
- Embryo, The Control of Hair and Feather Pigmentation as Revealed by Grafting Melanophores in the Embryo, 598
- EMERSON, G V Traumatic Arteriovenous Fistula, 942
- ENGEL, W J Pheochromocytoma with Hypermetabolism, 61
- ERB, WILLIAM H A Comparison of the Results of Roentgen Rays, Sulfanilamide and Serum Therapy in Experimental Gas Gangrene in the Pigeon, 713
- Esophagus, Cancer of the Cervical, 86
- EVANS, EVERETT I A Study of the "Shock Dying" Action of the Barbiturates, 658
- EVERETT, CLYDE Peritonitis Due to Perforation of an Infected Urachus Cyst, 154
- Expansion Reamer, 957
- Experimental Approach to the Problem of Menstrual Disorders, 604
- Extradural Hemorrhage in the Anterior Cranial Fossa, 821
- Extralaryngeal Division of the Recurrent Laryngeal Nerve, 251

F

- Fellowships, Announcement of, in Medicine and Public Health, 597
- Femoral and Iliac Arteries, A Complicated Case of Aneurysm Involving the, 708
- FERRER, JOSE M Primary Abscess of the Liver due to Anaerobic Nonhemolytic Streptococcus, 217
- Filtration, The Preparation of Nonpyrogenic Infusion and other Intravenous Fluids by Adsorptive, 412
- FINE, JACOB Recent Experiences with Thrombophlebitis of the Lower Extremity and Pulmonary Embolism, 574
- FINESTONE, EDWARD O Urinary Extravasation (Periurethral Phlegmon), 109
- FISHER, A MURRAY Duodenal Tumor of Unusual Character, 864
- Fistula, Arteriovenous, 470, Spontaneous External Biliary, 931, Traumatic Arteriovenous, 942
- Foot and Leg, Sympathetic Denervation Limited to the Blood Vessels of the, 476
- Forceps, A New Rectosigmoidal Biopsy, 637
- Fossa, Extradural Hemorrhage in the Anterior Cranial, 821

Fracture, Clavicle, Treated with Skeletal Traction, 950

Fractures of the Lower Leg Noninfective Gangrene Following, 721, Of the Olecranon, The Treatment of, by Longitudinal Screw or Nail Fixation, 293

FRANK, HOWARD A Recent Experiences with Thrombophlebitis of the Lower Extremity and Pulmonary Embolism, 574

G

GALLAGHER, PAUL Calcified Unilocular Cyst of the Spleen, 933

Gangrene and Thrombosis of Right Arm, Associated with Polycythemia Vera Its Relation to 'Effort Thrombosis,' 184, Following Fractures of the Lower Leg, Noninfective, 721

GANNON, JAMES, JR Closure of the Bronchus Following Total Pneumonectomy, 481

GARLOCK, JOHN H Regional Ileitis, 906

Gastrectomy in the Treatment of Gastroduodenal Ulcer, Recurrent Ulceration Following Subtotal, 729

Gastrointestinal Tract, Metabolic Studies in Patients with Cancer of the, 924

GAULF, JOSEPH T Production of a Thrombotic Barrier in the Treatment of Varicose Veins, 271

GERRIE JOHN W A Practical Concept for the Treatment of Major and Minor Burns, 641

GIBBONS, MARJORIE M A Simple Method of Plasma Protein Estimation, 426

GINZBURG, LEON Regional Ileitis, 906

Gland, Adenolymphoma of the Parotid, 43

GLASER, MARK ALBERT The Electroencephalographic Diagnosis of Subdural Hemorrhage, 452

GLOVER, D M Multiple Atresia of the Small Intestine, 337

Gout, Mediastinal, 795

GORDIMER, HARRY Postoperative Thromboembolization, 175

GOTTSCHALK ROBERT A Neurosurgical Head rest, 954

GRACE, EDWIN J Control of Massive Esophageal Hemorrhage Secondary to Liver Damage (Cirrhosis) by Ligation of the Coronary Vein and Injection of Sodium Morrhuate, 387

Grafting in the Treatment of Burns, Immediate Skin, 445

GREENE BARNETT A Posterior Pituitary Extract in Anesthesiology, 898

GRINNFLL, ROBERT S The Lymphatic and Venous Spread of Carcinoma of the Rectum, 200

GROSS, SIDNEY W Extradural Hemorrhage in the Anterior Cranial Fossa, 821

GURD, FRASER B A Practical Concept for the Treatment of Major and Minor Burns, 641

H

HAAGENSEN, C D Carcinoma of the Breast I—Results of Treatment, 801

HAAR, EDMUND Meningocele Spinaalis Traumatica Spuria, 150

Hamartoma of the Ileum with Intussusception, Myoepithelial, 355

HARPER FRED R Traumatic Diaphragmatic Hernia With Complete Tearing of the Mediastinal Pleura, 938

HARRISON, CARRINGTON Immediate and Late Results of Perforation of Peptic Ulcer, 194

HAYNES, ANNE Observations on the Failure of Heparin to Inhibit the Clotting of Blood *in vitro* by Staphylococci, 430

Head rest, Neurosurgical, 954

Heart, Intrapericardial Teratoma and a Tumor of the, 161

Hemangioma of the Ileum, 945

Hemangioepicytoma, 26

Hemisection of the Mandible for Recurrent Adenomatous, 277

Hemorrhage, Control of Massive Esophageal, Secondary to Liver Damage (Cirrhosis) by Ligation of the Coronary Vein and Injection of Sodium Morrhuate, 387, Electroencephalographic Diagnosis of Subdural, 452, In the Anterior Cranial Fossa, Extradural, 821

Hemorrhagic Cyst of the Spleen, 103

HEMPLEMAN, LOUIS H, JR The Pathogenesis of Mixed Tumors of the Salivary Gland Type, 34

Heparin, Observations on the Failure of, to Inhibit the Clotting of Blood *in vitro* by Staphylococci, 430

Hepatic Duct, Spontaneous Rupture of a Normal, 137

"Hepatorenal Syndrome," Severe Trauma to the Liver with, 223

Hernia with Osteoperiosteal Transplant, Repair of Direct Inguinal, 259, Spigelian, 405, Traumatic Diaphragmatic, With Complete Tearing of the Mediastinal Pleura, 938

Herniae, Sliding and other Large Bowel, 394

HELD, CHARLES GORDON The Increasing Useful-
ness of the Devine Colostomy in Left Colon
and Rectal Surgery, 913

HINTON, DRURY Recurrent Volvulus of the Sig-
moid Colon, 147

HINTON, J WILLIAM Extralaryngeal Division of
the Recurrent Laryngeal Nerve, 251

Hip, Invasion of the Bony Pelvis by Carcinoma
of the Cervix Uteri as a Cause of Pathologic
Central Dislocation of the, 1

HODES, PHILIP J A Comparison of the Results
of Roentgen Rays, Sulfanilamide and Serum
Therapy in Experimental Gas Gangrene in the
Pigeon, 713

HOLLOWAY, JOHN W Hemisection of the Man-
dible for Recurrent Adamantinoma, 277

HORNE, S F Cluvelhier Baumgarten Syndrome
(Splenomegaly, Portal Hypertension and Patent
Umbilical Vein), 860

HOWARD, FREDERICK S Severe Trauma to the
Liver with "Hepatorenal Syndrome," 223

Hypermetabolism, Pheochromocytoma with, 61

Hypertension, Adrenalin Producing Pheochromoc-
ytoma of the Adrenal Associated with, 54

Hyperthyroidism, Role of Infection in the Patho-
genesis of Liver Necrosis in, 851

I

Ileitis, Regional, 906

Ileum, Hemangioma of the, 945, Myoepithelial
Hamartoma of the, with Intussusception, 355

Iliac and Femoral Arteries, A Complicated Case
of Aneurysm Involving the, 708

Immediate and Late Results of Perforation of
Peptic Ulcer, 194

IMPINK, ROBERT R Atresia of the Duodenum,
334

Increasing Usefulness of the Devine Colostomy
in Left Colon and Rectal Surgery, 913

Infection, Role of, in the Pathogenesis of Liver
Necrosis in Hyperthyroidism, 851

Inguinal Hernia with Osteoperiosteal Transplant,
Repair of Direct, 259

Injuries, Chest, 668

Intestinal Obstruction in the Newborn, 321, In-
testinal Obstructions, 640

Intestine, Multiple Atresia of the Small, 337

Intrapericardial Teratoma and a Tumor of the
Heart Both Removed Operatively, 161

Invasion of the Bony Pelvis by Carcinoma of
the Cervix Uteri as a Cause of Pathologic
Central Dislocation of the Hip, 1

J

JACOBSON, SEYMOUR S Lt, M C An Attri-
bute Fascial Suture Needle, 315

Jejunal Ulcers, Multiple, Primary, Nonspecific,
with Chronic Duodenal Dilatation, 348

K

KENT, EDWARD M The Anatomic Approach to
Pulmonary Resection, 782

KIRSHBAUM, JACK D Adrenalin Producing Pheo-
chromocytoma of the Adrenal Associated with
Hypertension, 54

KLEINBURG, SAMUEL An Expansion Reamer, 957

KOPPELMAN, HAROLD Primary Carcinoma of the
Duodenum, 738

L

Lamp to Warm Moist Compresses, The Use of
a, 776

LAMPSON, R STARR Acute Pancreatitis, 367

LATTIN, BERTON Successful Closure of an Ar-
teriovenous Aneurysm Involving the Left In-
nominate Vein and the Left Common Carotid
Artery, 700

LEE, WALTER ESTELL Review of A Manual of
the Treatment of Fractures, 320, Review of
China's Health Problems, by, 960, Review of
Intestinal Obstructions, by, 640

Leg, Noninfective Gangrene Following Fractures
of the Lower, 721, And Foot, Sympathetic
Denervation Limited to the Blood Vessels of
the, 476

Lesions of the Astragalus, Less Common, 891

Less Common Lesions of the Astragalus, 891

LESTROHAN, PAUL Urologic Complications of
Cancer of the Rectum, 6

LEWIS, KENNETH M The Stader Reduction
Splint, 623

LEWIS, RAYMOND W Less Common Lesions of
the Astragalus, 891

LEWISON, EDWARD F, CAPTAIN, M C Rayable
Gauze, 311

LICHTENSTEIN, GEMMA M Cholecystectomy with
out Drainage, 928

- Liver, Massive Rupture of the, 827, Necrosis in Hyperthyroidism, Role of Infection in the Pathogenesis of, 851, Primary Abscess of the, Due to Anaerobic Nonhemolytic Streptococcus, 217, Severe Trauma to the, with "Hepatorenal Syndrome," 223, Solitary Nonparasitic Cyst of the, 751
- LONG, LEONARD Arteriovenous Fistula, 470
- LUNDQUIST DELL THEODORE The So called "Common Iliac Vein" of the Rabbit, 952
- Lymphatic and Venous Spread of Carcinoma of the Rectum, 200
- Lymphedema of the Arm Following Radical Mastectomy for Carcinoma of Breast, 816

M

- MACAUSLAND, W RUSSELL The Treatment of Fractures of the Olecranon by Longitudinal Screw or Nail Fixation, 293
- MACFEE, WILLIAM F Pilonidal Cysts and Sinuses A Method of Wound Closure, 687
- MAGE, SIGMUND Recurrent Ulceration Following Subtotal Gastrectomy in the Treatment of Gastroduodenal Ulcer, 729
- Malignant Degeneration of Neurofibromata of Peripheral Nerve Trunks (von Recklinghausen's Disease), 81, Teratoma of the Arm, 948
- Mandible, Hemisection of the, for Recurrent Adamantinoma, 277
- MASON, JAMES B A Large Gastric Ulcer, 342,
- Massive Rupture of the Liver, 827
- Mastectomy for Carcinoma of Breast, Lymphedema of the Arm following Radical, 816
- MATHESON, N M Invasion of the Bony Pelvis by Carcinoma of the Cervix Uteri as a Cause of Pathologic Central Dislocation of the Hip, 1
- MAY, HANS The Regeneration of Joint Transplants and Intracapsular Fragments, 297
- MCCARRELL JANE D A Study of the "Shock Delaying" Action of the Barbiturates, 658
- MCCLURE, ROY D Cysts of the Spleen, 98
- MCCORCKLE H Severe Trauma of the Liver with 'Hepatorenal Syndrome,' 223
- MCCULLAGH, E PERRY Pheochromocytoma with Hypermetabolism, 61
- McKATTRICK, CARL A A Practical Consideration of Open Pneumothorax under Sodium Evipal, Sodium Pentothal, and Ether Anesthesia, 553
- McLAUGHLIN, EDWARD FRANCIS Thrombosis and Gangrene of Right Arm, Associated with Polycythemia Its Relation to "Effort Thrombosis," 184
- Mediastinal Goiter, 795
- Medicine, Announcement of Fellowships in, 597
- MEIROWSKY, ARNOLD Studies on the Use of Metals in Surgery, Part II, 763
- Melanophores in the Embryo, The Control of Hair and Feather Pigmentation as Revealed by Grafting, 598
- Meningocele Spinalis Traumatica Spuria, 150
- Menstrual Disorders, An Experimental Approach to the Problem of, 604
- Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract, 924
- MILCH, HENRY So called Dislocation of the Lower End of the Ulna, 282
- MIRIZZI, PROF, P L A Study of the Bacteriology of the Common Bile Duct in Comparison with the other Extrahepatic Segments of the Biliary Tract, 360
- MOORE, RICHMOND L Pulmonary Abscess—A Surgical Problem, 373
- MOSSBERGER, JOSEPH I Calcified Unilocular Cyst of the Spleen, 933
- MOYER CARL A A Practical Consideration of Open Pneumothorax under Sodium Evipal, Sodium Pentothal, and Ether Anesthesia, 553
- MULLEN, THOMAS F Urologic Complications of Cancer of the Rectum, 6
- MUNROE, H STOKES, JR Solitary Nonparasitic Cyst of the Liver, 751
- MURRAY, MARGARET R Hemangiopericytoma, 26
- Myoepithelial Hamartoma of the Ileum with Intussusception, 355
- Myotomy in the Repair of Divided Flexor Tendons, The Use of, 461

N

- Needle, Atraumatic Fascial Suture, 315
- NELSON, O A Siphon Drainage for Suprapubic Cystostomy, 159
- Nerve, Extralaryngeal Division of the Recurrent Laryngeal, 251
- Nervous System, Central, Platybasia with Involvement of the Central, 231
- Neurofibromata of Peripheral Nerve Trunks, Malignant Degeneration of, (von Recklinghausen's Disease), 81
- Neurogenic Shock, 610

- Neurosurgical Head rest, 954
- Newborn, Intestinal Obstruction in the, 321
- New Rectosigmoidal Biopsy Forceps, 637
- NICHOL, WILLIAM W Traumatic Arteriovenous
Fistula, 942
- NICKEL, WILLIAM F, JR Paget's Disease of
the Nipple, 19
- Nipple, Paget's Disease of the, 19
- Noninfective Gangrene Following Fractures of
the Lower Leg, 721

O

- Obstruction, Intestinal, in the Newborn, 321
- Occlusion of the Portal Vein and Hepatic Artery,
Temporary, 833
- Olecranon, The Treatment of Fractures of the,
by Longitudinal Screw or Nail Fixation, 293
- OFFENHEIMER, GORDON D Common Duct Ob-
struction Due to Primary Carcinoma of the
Cystic Duct, 141
- Osteoperiosteal Transplant, Repair of Direct In-
guinal Hernia with, 259

P

- PACK, G T Metabolic Studies in Patients with
Cancer of the Gastrointestinal Tract, 924,
Sacrococcygeal Teratoid Tumor, 76
- Paget's Disease of the Nipple, 19
- Pancreatitis, Acute, 367
- PARKER, EDWARD F Myoepithelial Hamartoma
of the Ileum with Intussusception, 355
- Pathogenesis of Mixed Tumors of the Salivary
Gland Type, 34
- PEARSE, HERMAN E The Use of a Lamp to
Warm Moist Compresses, 776
- Pelvis, Invasion of Bony, by Carcinoma of the
Cervix Uteri as a Cause of Pathologic Central
Dislocation of the Hip, 1
- Peritoneoscopy, Postmortem, 843
- Peritonitis Due to Perforation of an Infected
Urachus Cyst, 154
- PHELPS, DORIS An Experimental Approach to
the Problem of Menstrual Disorders, 604
- PHENISTLER, DALLAS B Neurogenic Shock, 610
- Pheochromocytoma of the Adrenal Associated with
Hypertension, Adrenalin Producing, 54, With
Hypermetabolism, 61
- PILCHER, LEWIS S Massive Rupture of the
Liver, 827

- Pilonidal Cysts and Sinuses A Method of Wound
Closure, 687
- Pituitary Extract in Anesthesiology, Posterior,
898
- Plasma Protein Estimation, A Simple Method of,
426
- Platybasia with Involvement of the Central Ner-
vous System, 231
- PLAUT, JULES ALAN Adenolymphoma of the
Parotid Gland, 43
- Pneumonectomy, Effect of upon the Cardiopul-
monary Function in Adult Patients, 532
- Pneumothorax, The Practical Consideration of
Open, under Sodium Evipal, Sodium Pento-
thal, and Ether Anesthesia, 553
- Polycythemia Vera, Gangrene and Thrombosis of
Right Arm Its Relation to "Effort Throm-
bosis," 184
- Posterior Pituitary Extract in Anesthesiology,
898
- Postmortem Peritoneoscopy, 843
- Postoperative Thromboembolization, 175
- Practical Concept for the Treatment of Major
and Minor Burns, 641, Consideration of Open
Pneumothorax under Sodium Evipal, Sodium
Pentothal, and Ether Anesthesia, 553
- Preparation of Nonpyrogenic Infusion and other
Intravenous Fluids by Adsorptive Filtration,
412
- Primary Abscess of the Liver Due to Anaerobic
Nonhemolytic Streptococcus, 217, Carcinoma of
the Duodenum, 738
- PRITCHARD, J E A Practical Concept for the
Treatment of Major and Minor Burns, 641
- Production of a Thrombotic Barrier in the Treat-
ment of Varicose Veins, 271
- Public Health, Announcement of Fellowships in,
597
- PULASKI, EDWIN J Primary Abscess of the
Liver due to Anaerobic Nonhemolytic Strepto-
coccus, 217
- Pulmonary Reaction, Anatomic Approach to, 782
- Punch for Cutting Cottonoid Sponges for use in
Neurosurgical Operations, 318

R

- RANKIN, L M Spontaneous External Biliary
Fistula, 931
- RAY, BRONSON S Platybasia with Involvement
of the Central Nervous System, 231

- Reamer, Expansion, 957
- Recent Experiences with Thrombophlebitis of the Lower Extremity and Pulmonary Embolism, 574
- Rectal and Left Colon Surgery, The Increasing Usefulness of the Devine Colostomy in, 913
- Rectosigmoidal Biopsy Forceps, A New, 637
- Rectum, The Lymphatic and Venous Spread of Carcinoma of the, 200, Urologic Complications of Cancer of the, 6
- Recurrent Ulceration Following Subtotal Gastrectomy in the Treatment of Gastroduodenal Ulcer, 729
- REED, FRANCIS A Volvulus of the Cecum, 874
- Regeneration of Joint Transplants and Intracapsular Fragments, 297
- Regional Ileitis, 906
- REICH, NATHANIEL L Spontaneous Rupture of a Normal Hepatic Duct, 137
- Repair of Direct Inguinal Hernia with Osteoperiosteal Transplant, 259
- Resection, Anatomic Approach to Pulmonary, 782
- RHOADS, C P Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract, 924
- RIENHOFF WILLIAM F Closure of the Bronchus Following Total Pneumonectomy, 481
- RIGDON R H Effect of Heparin on Phagocytosis by the Cells of the Reticuloendothelial System, 122
- Observations of the Failure of Heparin to Inhibit the Clotting of Blood *in vitro* by Streptococci, 430, RILEY, RICHARD L Cardiovascular Dynamics in Surgical Shock, 127
- RIVER, LOUIS P Spigelian Hernia, 405, Volvulus of the Cecum, 874
- Roentgen Rays, Results of Sulfanilamide and Serum Therapy in Gas Gangrene, 713
- Role of Infection in the Pathogenesis of Liver Necrosis in Hyperthyroidism, 851
- ROWE, M JOHN Clavicle Fracture Treated with Skeletal Traction, 950
- Rupture of the Liver, Massive, 827
- S
- ST JOHN, IORDACE B Primary Abscess of the Liver due to Anaerobic Nonhemolytic Streptococcus, 217
- SAVITSKY NATHAN Extradural Hemorrhage in the Anterior Cranial Fossa, 821
- SCHACHTER, RUBIN J Neurogenic Shock, 610
- SCHIRANTZ, I S Effect of Heparin on Phagocytosis by the Cells of the Reticuloendothelial System, 122
- SEALY, W C Role of Infection in the Pathogenesis of Liver Necrosis in Hyperthyroidism, 851
- Serum Therapy, Roentgen Rays and Sulfanilamide, Treatment of Gas Gangrene, 713
- Severe Trauma to the Liver with "Hepatorenal Syndrome," 223
- SEWELL, ROBERT L Spontaneous Amputation, 155
- SHACKELFORD RICHARD T Duodenal Tumor of Unusual Character, 864
- SHAPIRO, SHEPARD Postoperative Thromboembolization, 175
- SHERMAN, IRWIN Closure of the Bronchus Following Total Pneumonectomy, 481
- SHERWIN BENJAMIN Postoperative Thromboembolization, 175
- Shock, Cardiovascular Dynamics in Surgical, 127, Neurogenic, 610
- "Shock Delaying" Action of the Barbiturates, A Study of the, 658
- Sinuses, Pilonidal Cysts and A Method of Wound Closure, 687
- Siphon Drainage for Suprapubic Cystostomy, 159
- SJAARDEMA, HENDRIKUS The Electroencephalographic Diagnosis of Subdural Hemorrhage, 452
- SMITH, SIMMONS Multiple Atresia of the Small Intestine, 337
- So called "Common Iliac Vein" of the Rabbit, 952
- Solitary Nonparasitic Cyst of the Liver, 751
- SPEED, KELLOGG Malignant Degeneration of Neurofibromata of Peripheral Nerve Trunks (von Recklinghausen's Disease), 81
- Spigelian Hernia, 405
- Spleen, Calcified Unilocular Cyst of the, 933, Hemorrhagic Cyst of the, 103
- Splint, The Stader Reduction, 623
- Sponges, Cottonoid, Punch for Cutting, for use in Neurosurgical Operations, 318
- Spontaneous Amputation, 155, External Biliary Fistula, 931, Rupture of a Normal Hepatic Duct, 137
- STADER OTTO The Stader Reduction Splint, 623
- Stader Reduction Splint, 623

- STANDARD, SAMULL Lymphedema of the Arm Following Radical Mastectomy for Carcinoma of Breast, 816
- STARR, ARNOLD Recent Experiences with Thrombophlebitis of the Lower Extremity and Pulmonary Embolism, 574
- STEINER, CHARLES A Recurrent Volvulus of the Sigmoid Colon, 147
- STOUT, A P Carcinoma of the Breast I—Results of Treatment, 801, Hemangiopericytoma, 26
- Studies on the Use of Metals in Surgery, Part II, 763
- Study of the "Shock Delaying" Action of the Barbiturates, 658
- Successful Closure of an Arteriovenous Aneurysm Involving the Left Innominate Vein and the Left Common Carotid Artery, 700
- Sulfanilamide, Serum Therapy and Roentgen Rays in Treatment of Gas Gangrene, 713
- SUTHERLAND, ROSS Clavicle Fracture Treated with Skeletal Traction, 950
- SWARTLEY, WILLIAM B Thrombosis and Gangrene of Right Arm, Associated with Polycythemia Vera Its Relation to "Effort Thrombosis," 184
- SWEET, RICHARD H Transthoracic Resection of Tumors of the Esophagus and Stomach (Case Reports), 566
- Sympathetic Denervation Limited to the Blood Vessels of the Leg and Foot II, 476
- Syndrome, Cruveilhier Baumgarten, 860
- T**
- TARNOWER, HERMAN Successful Closure of an Arteriovenous Aneurysm Involving the Left Innominate Vein and the Left Common Carotid Artery, 700
- TAYLOR, FREDERIC W A Simple Method of Plasma Protein Estimation, 426
- Temporary Occlusion of the Portal Vein and Hepatic Artery, 833
- Tendons, The Use of Myotomy in the Repair of Divided Flexor, 461
- Teratoma of the Arm, Malignant, 948, And a Tumor of the Heart, Intrapericardial, 161
- Thrombo embolization, Postoperative, 175
- Thrombophlebitis of the Lower Extremity and Pulmonary Embolism, Recent Experiences with, 574
- Thrombosis and Gangrene of Right Arm, Associated with Polycythemia Vera Its Relation to "Effort Thrombosis," 184
- Traction, Clavicle Fracture Treated with Skeletal, 950
- Transplants Regeneration of Joint and Intracapsular Fragments, 297
- Transthoracic Resection of Tumors of the Esophagus and Stomach, (Case Reports), 566
- Trauma to the Liver with "Hepatorenal Syndrome," Severe, 223
- Traumatic Arteriovenous Fistula, 942, Diaphragmatic Hernia With Complete Tearing of the Mediastinal Pleura, 938
- Treatment of Fractures of the Olecranon by Longitudinal Screw or Nail Fixation, 293
- FUI, CO The Preparation of Nonpyrogenic Infusion and other Intravenous Fluids by Adsorptive Filtration, 412
- Tumor of Unusual Character, Duodenal, 864, And a Teratoma of the Heart, Intrapericardial, 161
- Tumors of the Esophagus and Stomach, Transthoracic Resection of, 566, Of the Salivary Gland Type, The Pathogenesis of Mixed, 34, The Surgery of Pancreatic, 799
- TURELL, ROBERT A New Rectosigmoidal Biopsy Forceps, 637
- U**
- Ulcer, Immediate and Late Results of Peptic, 194, Large Subacute Gastric, 342, Recurrent Ulceration Following Subtotal Gastrectomy in the Treatment of Gastroduodenal, 729
- Ulceration Following Gastrectomy in the Treatment of Gastroduodenal Ulcer, Recurrent, 729
- Ulcers, Jejunal, Multiple, Primary, Nonspecific, with Chronic Duodenal Dilatation, 348
- Ulna, So called Dislocation of the Lower End of the, 282
- Urachus Cyst, Peritonitis Due to Perforation of an Infected, 154
- Urologic Complications of Cancer of the Rectum, 6
- Use of a Lamp to Warm Moist Compresses, 776
- V**
- VALK, H L Cruveilhier Baumgarten Syndrome (Splenomegaly, Portal Hypertension and Patent Umbilical Vein), 860
- Varicose Veins, Production of a Thrombotic Barrier in the Treatment of, 271
- VEAL, J ROSS Repair of Direct Inguinal Hernia with Osteoperiosteal Transplant, 259
- Vein and Hepatic Artery, Occlusion of the Portal, 833, Left Innominate, Successful Closure

- of an Arteriovenous Aneurysm Involving the Left Common Carotid Artery, 700
- Veins, Production of a Thrombotic Barrier in the Treatment of Varicose, 271
- von Recklinghausen's Disease, Malignant Degeneration of Neurofibromata of Peripheral Nerve Trunks, 81

W

- WARREN, SHIELDS Leiomyosarcoma of the Uterus, 882
- WATSON, WILLIAM L Cancer of the Cervical Esophagus, 86
- WEEDER, S DANA Thrombosis of Right Arm, Associated with Polycythemia Vera Its Relation to "Effort Thrombosis," 184
- WEEKS, CARNES Extralaryngeal Division of the Recurrent Laryngeal Nerve, 251
- WEST, JOHN PETTIT Paget's Disease of the Nipple, 19
- WHELOCK, MARK C Leiomyosarcoma of the Uterus, 882
- WHIPPLE, ALLEN O Review of the Surgery of Pancreatic Tumors, by, 799
- WILLIER, B H The Control of Hair and Feather Pigmentation as Revealed by Grafting Melanophores in the Embryo, 598
- WOMACK, NATHAN A The Pathogenesis of Mixed Tumors of the Salivary Gland Type, 34
- WYLIE, ROBERT H Cardiocirculatory Dynamics in Surgical Shock, 127

Y

- YOUNG, FORREST Immediate Skin Grafting in the Treatment of Burns, 445

Z

- ZEMAN, ERWIN, 1ST LT A Large Subacute Gastric Ulcer, 342

